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Synthesis, structure and chirality of some neutral cobalt (III) complexes

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SYNTHESIS, STRUCTURE AND CHIRALITY OF SOME NEUTRAL COBALT(III) COMPLEXES

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This Dissertation submitted by David J. Seematter in partial fulfillment of the requirements for the Degree of Doctor of Philosophy from the University of North Dakota is hereby approved by the Faculty Advisory Committee under whom the work has been done.

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ABSTRACT

Structures are assigned to the six stereoisomers of the complex 2,4-pentanedionatobis(S-alaninato)cobalt(III) and to the diastereomers of bis(2,4-pentanedionato)S-aminoacidatocobalt(III), where the S-amino acid is S-alanine, S-valine, N-methyl-S-alanine and N-methyl-S-valine. Adsorption column chromatography on alumina was used to separate these neutral complexes which are soluble in water and non-aqueous solvents. Electronic absorption spectra are interpreted in assigning geometric isomers and C-O bond anisotropic deshielding arguments are applied to proton nmr chemical shifts in making chiral assignments of the helical diastereomers. A comparison is made between C-O bond deshielding and N-D steric compression. The proton nmr assignments are shown to be independent of the solvent used in measuring chemical shifts and agree with assignments made from circular dichroism spectra in every case. No stereospecificity was observed in these systems or for the complexes bis(2,4-pentanedionato)aminoacidato-cobalt(III) where the amino acid is sarcosine, S-proline and S-serine. A convenient, high yield synthesis of tris(2,4-pentanedionato)-rhodium(III) is reported.

INTRODUCTION

Historical Background

The coordination theory outlined by Werner in 1891[1] provided a basis for the development of modern day structural inorganic chemistry. However, substantiation of Werner's ideas required many years of careful experimentation by a number of people to adequately test and correct the theory. Throughout this entire period, the observation of optical activity in metal complexes has been tantamount to understanding the structures of coordination compounds. In particular the progress of theories and techniques concerning optical activity in octahedral coordination complexes is of interest.

Cotton had observed the anomalous optical activity of copper tartrate salts in 1896[2] and Werner himself resolved the first helical coordination compounds by 1912, $[Co(en)_2X_2]^{+3}$ and $[Co(en)_3]^{3+}$.[4] In order to demonstrate to his critics that the optical activity of metal complexes was not in some manner due to the presence of asymmetric carbon in the ligands, Werner resolved a completely inorganic helical complex in 1914.[5] During this period optical activity was measured only in terms of the rotational strength of the complexes at various wavelengths of visible polarized light.

Meanwhile Lifschitz[6] in 1925 and Jaeger[7] in 1928 reported the first observed stereospecific behavior of metal complexes containing optically active ligands. Much of this work has been improved upon, however not until modern methods of analysis were available (vida infra).

In the early 1930's, Mathieu[8] and Kuhn[9] studied the optical rotary dispersion (ORD) and circular dichroism (CD) of a great number of optically active metal complexes. As a result of this work the helical relationships of complexes were predictable for the first time by spectroscopic techniques. From this time until the 1950's there was little interest in ORD and CD of metal complexes. In the mid 1930's Bailar[10] and in the 1950's Basolo[11] were very active in the area of reaction mechanisms. Bailar proposed, among other things, the Walden inversion and Basolo found the SN1 process occurred with octahedral complexes much like the mechanisms known for organic reactions.

Moffitt[12] proposed a theory of optical rotatory power involving d-d orbital electronic transitions of metal complexes in 1956 thus stimulating new interest in CD. Crystal field theory was adapted to explain the absorption spectra and optically active d-d bands of complexes by a number of people: Ilse and Hartman, Ballhausen, Jorgensen, Cotton, Liehr, Piper and others.[1] In 1957 Saito et al.,[13] published the single crystal X-ray structure of $(+)_D$-$[Co(en)_3]^{3+}$ which established the basis for assigning the helical arrangement of metal complexes by a comparative

CD method. Mason and Douglas were very active in assigning the chirality of optically active metal complexes by CD in the 1960's.[14]

About the same time, Dwyer, Mellor and Sargeson[15] reported several extensive studies on the stereospecific behavior of complexes containing optically active ligands. This work revealed that earlier claims of complete stereospecificity imparted by optically active diamines were in error. Bailar and Corey[16] theoretically explained ring conformations in support of Dwyer's work and Douglas[17] has developed the vicinal effect in CD to explain the additive properties of multiple optically active centers.

More recently several methods to assign the helical configuration of optically active metal complexes have been reported. Hidaka et al.,[18] have used the exciton ultraviolet technique originated by Bosnich[19] to assign chirality of metal complexes. In 1965 proton nuclear magnetic resonance (pmr) was used in the helical assignment of metal complexes by Cooke and Dabrowiak.[20] In the next few years, Brushmiller et al.,[21] developed a pmr method to predict the chirality of metal complexes.

At the present time there is much interest in the helical structure of octahedral complexes. Many X-ray structures have been reported[22] and new methods such as X-ray powder patterns[23] and Co^{59}nmr[24] are being investigated as structural tools for predicting the stereochemistry of metal complexes.

Octahedral Metal Complexes

In order to discuss octahedral metal complexes in terms of their structure, some pertinent properties of metal ions and their complexes should be mentioned. Cotton and Wilkenson have thoroughly discussed these properties.[25]

The majority of transition metal complexes known contain metal ions with hexavalent coordination spheres. A metal ion of this type exhibits six equivalent sites for electron donor atoms arranged about the metal at the apexes of a regular octahedron. Thus the term "octahedral coordinate" is used to describe Co^{3+}, Cr^{3+}, Rh^{3+}, Ir^{3+}, Fe^{3+}, Ru^{3+} and Pt^{4+}, all of which can accommodate six ligand donor atoms. If the total electrical charge of the ligands is equal to the charge on the central metal atom the complex is neutral and is often called an inner complex. When the total ligand charge is more or less than the metal ion charge an ionic complex results and counter ions must be present thus forming a complex salt. Ionic complexes have been extensively studied in terms of their structure, reactions and mechanisms probably because of their convenient water solubility.[26] Most inner complexes, on the other hand, show limited solubility and can be categorized as one of two types, (1) soluble only in non-polar solvents or (2) slightly soluble in water and insoluble in non-polar solvents.

Ligands

Ligands encountered in octahedral complexes contain as many as six atoms that donate a pair of electrons to the central metal atom. For instance, EDTA with a total of six donor atoms is termed a sexadentate ligand and ammonia with a single donor atom is called a unidentate ligand. However, this discussion will be limited to bidentate ligands which have two donor atoms and form small ring systems or chelate rings when coordinated to a metal atom. The rings usually contain a total of five or six atoms including the metal atom. Smaller chelate rings tend to be very strained and larger rings are uncommon because the ligand then preferentially bridges between two metal atoms.[27] For octahedral complexes a bidentate ligand spans two adjacent or cis positions about the metal atom and cannot span two non-adjacent or trans sites due to the larger distances involved.[27]

Classification of Bidentate Ligands

For purposes of clarity in discussing the stereochemistry of complexes it will be convenient to classify bidentate ligands in three categories: symmetric, unsymmetric and asymmetric.

Symmetric ligands

Symmetric bidentate ligands may be defined as ligands that, when coordinated to a metal atom generate a chelate ring which possesses a

C_2 rotation axis extending from the metal atom through the center of the ligand as shown in Figure 1.

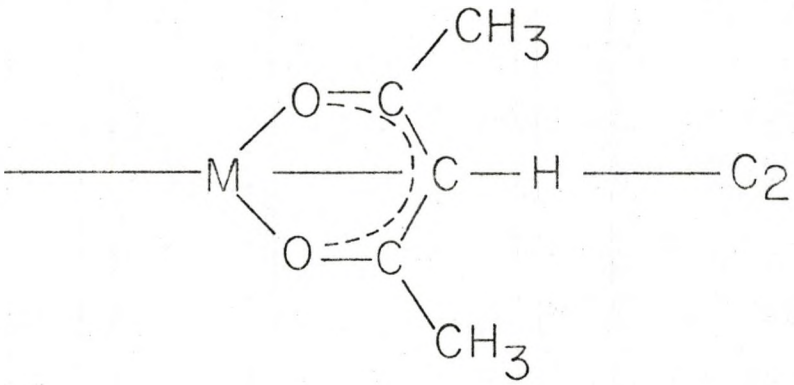


Fig. 1.--Symmetry of a coordinated acac ligand

In the case of acac there is also a plane of symmetry defined by the metal and the two oxygen donor atoms. Other examples of well known symmetric bidentate ligands, also containing a plane of symmetry, are ox, hfa, dipy and o-phen. The ligand en is an example of a symmetric ligand, which upon coordination, possesses no plane of symmetry.

Unsymmetric ligands

Unsymmetric bidentate ligands when coordinated to a metal atom generate a chelate ring which has no rotational symmetry but possess a plane of symmetry defined by the metal atom and the two donor atoms as shown in Figure 2. Another definition of an unsymmetric ligand would be that the donor atoms of the ligand are different as in gly or groups on the ligand cause the donor atoms to be non-equivalent as in tfa and ibn.

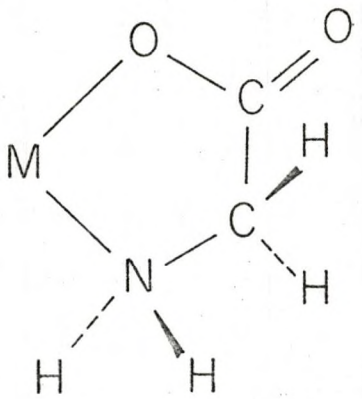


Fig. 2.--Symmetry of a coordinated gly ligand

Asymmetric ligands

Asymmetric bidentate ligands possess one or more asymmetric centers in the ligand and generally exhibit only C_1 symmetry upon coordination to a metal atom. A coordinated asymmetric S-amino acid (S-amac) ligand is illustrated in Figure 3. Special cases of asymmetric ligands such as R,R or S,S 2,3-diaminobutane (not the meso form) exhibit C_2 symmetry upon coordination. Thus the fundamental requirement of an asymmetric ligand is the coordinated ligand possess no S_2 or higher improper axis of symmetry. The R,S nomenclature of Cahn[28] is used to describe the asymmetric centers in the ligands.

Spatial Relationships of Tris-chelate Octahedral Complexes

Tris-chelate octahedral complexes are capable of exhibiting stereoisomerism (isomerism in space). Stereoisomers refer to molecules composed of the same atoms but differing in the spatial arrangement of

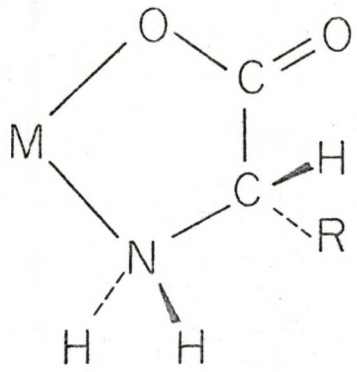


Fig. 3.--Symmetry of a coordinated S-amac ligand

these atoms and they are separated by an energy barrier. The energy barrier is required in order to slow the interconversion of the stereoisomers long enough to observe their individual existence by some experiment.[29] Stereoisomers may exist as enantiomers, diastereomers or geometric isomers and these are best described by using the above ligand classifications with some examples of stereoisomeric metal complexes.

Complexes with three symmetric ligands

An octahedral complex with three identical symmetric ligands is capable of existing in the two forms as shown in Figure 4 for $[Co(acac)_3]$. The isomers in Figure 4 are enantiomers because they are related as molecule and non-superimposable mirror image. Enantiomers may possess a proper axis (or axes) of rotation but may not exhibit an improper rotation axis. In fact the molecules in Figure 4 possess a C_3

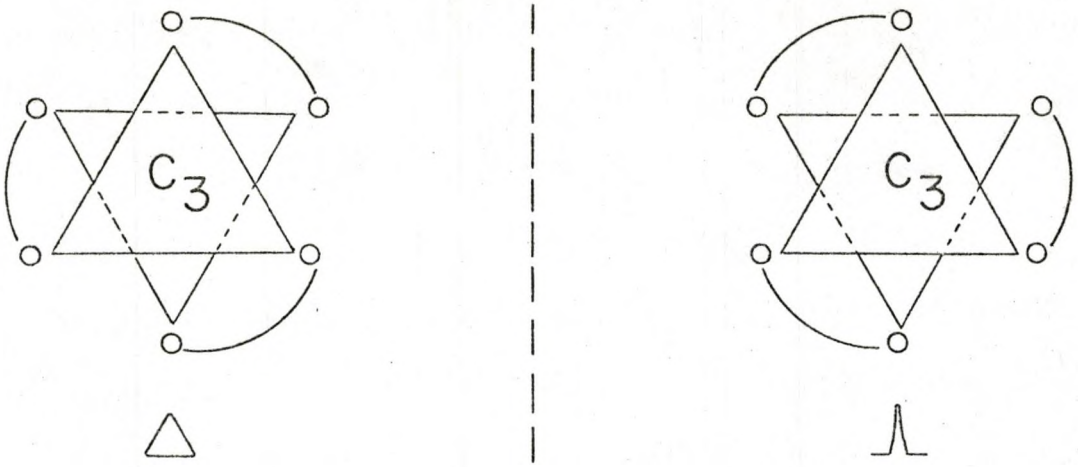


Fig. 4.--Enantiomers of $[Co(acac)_3]$

axis and $3C_2$ axes perpendicular to the C_3 axis. Thus the term dissymmetric is more desirable than asymmetric in describing molecules of this type.[14] It should be pointed out that a dissymmetric molecule can have one and only one non-superimposable mirror image.

The helical chirality or handedness of the complexes shown in Figure 4 is described by looking down the C_3 axis and observing the helical sense which the bidentate ligands impart to the complex. If the helix is right-handed or a clockwise rotation of the helix would cause the molecule to move away from the observer, the helix is designated Δ. If it is left-handed or a counter-clockwise rotation would cause the molecule to move away from the observer the helix is designated Λ. It is noteworthy that the helical sense observed along one of the C_2 axes perpendicular to the C_3 axis is just the reverse of the helical sense along the C_3 axis. This change in the helical sense between symmetry axes has produced a great deal of confusion in the nomenclature of

helical metal chelates.[30] However the method outlined here was proposed by the IUPAC in 1970.[31]

Enantiomers have identical scalar physical properties such as free energy, magnetic moment, solubility, etc., however they differ in directional or vector physical properties such as the absorption of circularly polarized light, the direction of rotation of plane polarized light, or interaction with another dissymmetric molecule. In fact enantiomers can be distinguished from one another only by techniques involving a directional or dissymmetric media. In the absence of such a media enantiomers are formed in equal amounts and appear to be identical.

Complexes with three unsymmetric ligands

Octahedral complexes containing three identical unsymmetric ligands exhibit two modes of coordination in terms of the spatial arrangement of the donor atoms around the central metal atom. Figure 5 illustrates the possible isomers of a complex containing three gly ligands. In Figure 5a the nitrogen donor atoms of all three gly ligands are coordinated adjacent to one another on a triangular face of the octahedron and the complex has C_3 symmetry. This arrangement is called the facial (fac) and cis form. In Figure 5b two of the nitrogen donor atoms are arranged in a non-adjacent manner and the complex has C_1 symmetry. This is termed meridional (mer) or trans coordination.

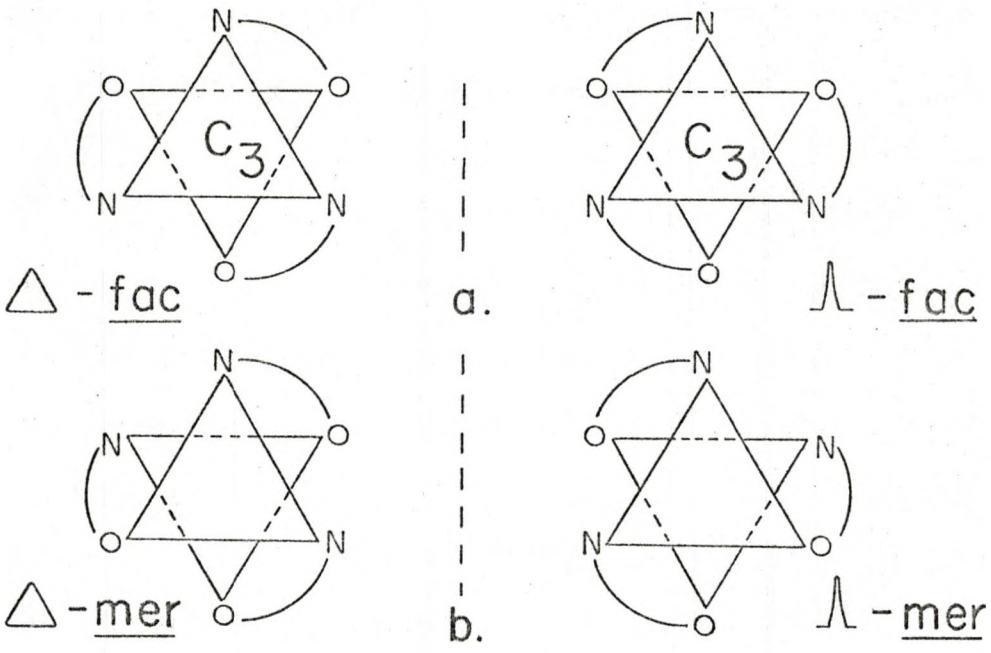


Fig. 5.--Possible isomers of $[Co(gly)_3]$

Facial and meridional coordination are examples of geometric isomerism in which the two forms exhibit different scalar physical properties. The most readily observable difference between geometric isomers is the unequal effect of the two modes of coordination on the crystal field splitting of the metal d orbitals. Thus geometric isomers of a complex often have different visible absorption spectra.[32]

Both geometric arrangements of the tris(gly) complex exist as △ and Λ enantiomeric pairs as shown in Figure 5. The helical chirality of the facial isomers is observed along the C_3 axis as previously described. For the meridional isomers which have no symmetry axis,

all three ligands are assumed to be identical and the helical chirality is observed along the pseudo C_3 axis.[31]

Complexes with three asymmetric ligands

Considering tris-type complexes with asymmetric ligands the situation becomes more complicated since all three forms of stereoisomerism are possible. For brevity and clarity this discussion will be limited to the facial geometry of a tris(amac) complex system in which only one form of the amino acid is present in any single stereoisomer. With these restrictions Figure 6 illustrates such a system.

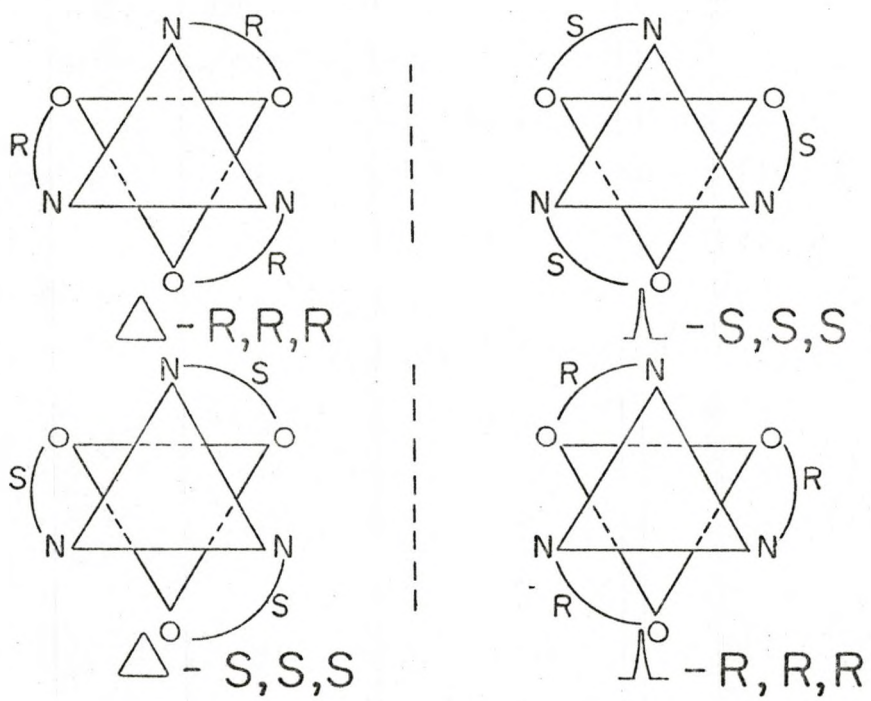


Fig. 6.--Possible isomers of fac-[Co(rac-amac)$_3$]

Two sets of enantiomers, Δ-R,R,R; Λ-S,S,S (a racemic pair) and Δ-S,S,S; Λ-R,R,R (a racemic pair) are possible. Each individual isomer possesses more than one source of dissymmetry (dissymmetry includes asymmetry); the helical chirality about the metal atom and the configuration at the asymmetric carbon atom of the amino acid ligands. Stereoisomers of the same geometry which contain the same types of dissymmetric groupings, some but not all of which are related as object and non-superimposable mirror image are called diastereomers.[14] Thus Δ-S,S,S and Λ-R,R,R are diastereomers of Δ-R,R,R because neither is the mirror image of Δ-R,R,R. A similar argument may be employed for each individual isomer shown in Figure 6. Each isomer is related to one other isomer enantiomerically and is related to the two remaining isomers diastereomerically.

As a practical approach to a system of this type, a method that reduces the total number of isomers is often employed. By introducing only S-amac in the preparation of the complexes, provided it does not racemize or invert under the reaction conditions, only two facial isomers are generated, Δ-S,S,S and Λ-S,S,S. This has the distinct advantage of eliminating enantiomer formation. An additional advantage is that diastereomers have different scalar physical properties and are therefore separated, identified and studied by scalar methods as opposed to more difficult and underdeveloped dissymmetric techniques required for enantiomers.

Stereoselectivity and stereospecificity

An important characteristic of diastereomers as well as geometric isomers is that they need not be produced in equimolar amounts from a reaction as is required for enantiomers. A reaction which leads to the formation of a non-statistical distribution of the possible stereoisomeric products is called a stereoselective synthesis. The observed stereoselectivity is either thermodynamic or kinetic in origin depending on whether the products are observed at the thermodynamic equilibrium or considerably before that occurs.[33] On the other hand a stereospecific synthesis is a reaction in which a given isomer of the reactant leads to one product (or one set of products) while another isomer of the same reactant leads to the opposite product (or products). All stereospecific reactions are necessarily stereoselective, however the converse is not true. As a result, reactions carried out with reactants which do not exhibit stereoisomerism can be stereoselective but not stereospecific.[34] A stereospecific synthesis involving optically active reagents has often been called an asymmetric synthesis.[34] For example, an asymmetric synthesis occurs in the formation of $[Co(pn)_3]^{3+}$ in which R-pn produces predominantly (97%) the Δ chirality and S-pn produces predominantly (97%) the Λ chirality of the complex.[35]

Complexes with two symmetric ligands and one unsymmetric ligand

Tris-chelate octahedral complexes containing mixed ligand substitution produce a variety of stereoisomeric situations. Consider a complex containing two symmetric acac ligands and one unsymmetric gly ligand. Only one geometric form is possible as shown in Figure 7. The isomers are enantiomeric and possess C_1 symmetry. The chiralities are

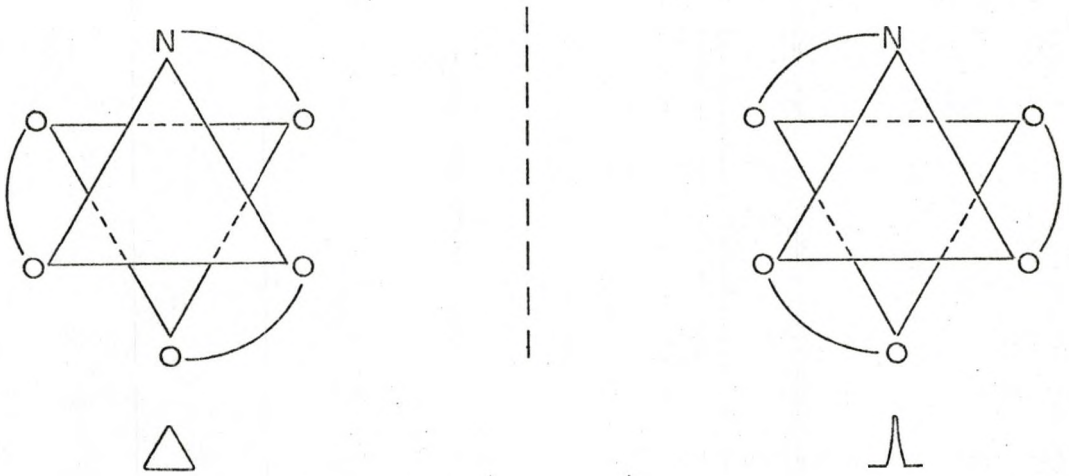


Fig. 7.--Possible isomers of $[Co(acac)_2(gly)]$

found with respect to the pseudo C_3 axis. Complex ions of this type are known for $[Co(ox)_2(gly)]^{2-}$[36] which is soluble in water while the inner complex $[Co(acac)_2(gly)]$[37] is soluble not only in water but also in polar non-aqueous solvents.

Complexes with two symmetric ligands and one asymmetric ligand

If two symmetric acac ligands and an asymmetric ligand such as racemic ala are coordinated to a metal ion, four stereoisomers are possible as shown in Figure 8. The system consists of two sets of

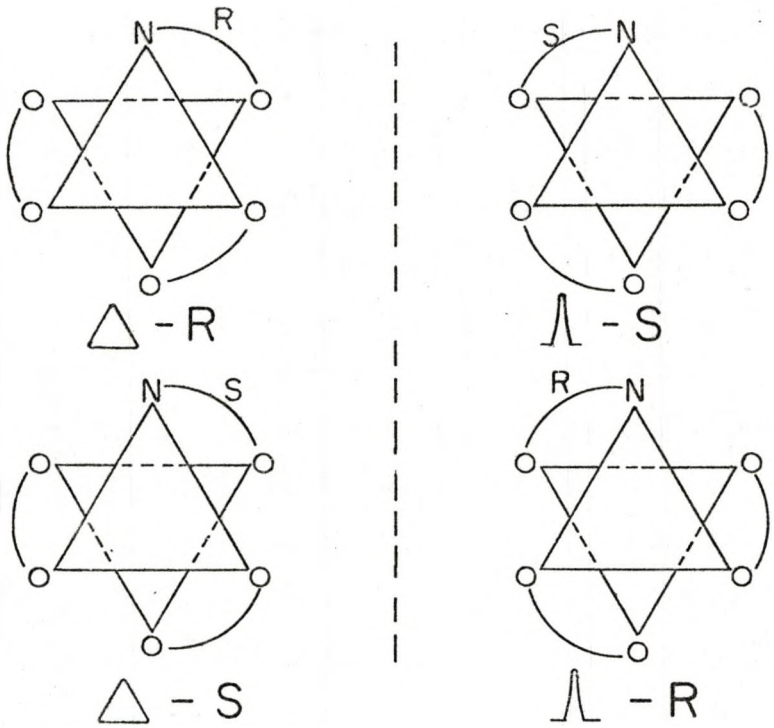


Fig. 8.--Possible isomers of $[Co(acac)_2(rac\text{-}amac)]$

enantiomers that are diastereomeric to one another and all the isomers have C_1 symmetry. If an S-amac is used to synthesize the complex the products are Δ -S and Λ -S diastereomers only. Systems of this type are known, for example: Δ and Λ -$[Co(ox)_2(S\text{-}amac)]^{2-}$[38, 39] and Δ and Λ -$[Co(en)_2(S\text{-}amac)]^{2+}$[40, 41] which are water soluble complex ions.

For $[Co(acac)_2(S\text{-}amac)]$[37] several systems have been prepared in which the inner complexes are soluble in water and also polar non-aqueous solvents.

Complexes with one symmetric ligand and two asymmetric ligands

Tris-type complexes containing one symmetric ligand and two asymmetric ligands give rise to a very interesting system of stereoisomers. Figure 9 illustrates such a system for $[Co(acac)(S\text{-}amac)_2]$. The complexes exist in three geometric forms, trans-N-C_2, cis-N-C_2 and cis-N-C_1. The geometry is described with respect to the arrangement of the nitrogen donor atoms and the symmetry of the molecule is indicated. The Δ and Λ forms for each geometry are diastereomers as no enantiomeric relationships can exist as long as the complex contains only an S-amac. Thus the six stereoisomers have different scalar physical properties and need not form in equal amounts. Systems of this type have been studied for $[Co(ox)(S\text{-}ala)_2]^-$[38, 42] and $[Co(ox)(S\text{-}ser)_2]^-$[43] which are water soluble complex ions. Wingert et al., have studied the neutral systems $[Co(acac)(S\text{-}val)_2]$[21] and $[Co(acac)(N\text{-}Me\text{-}S\text{-}ala)_2]$.[44]

Methods of Obtaining Pure Stereoisomers

Isolation of the stereoisomers of metal complexes, or of any molecule, requires that the stereoisomers obtained are capable of a

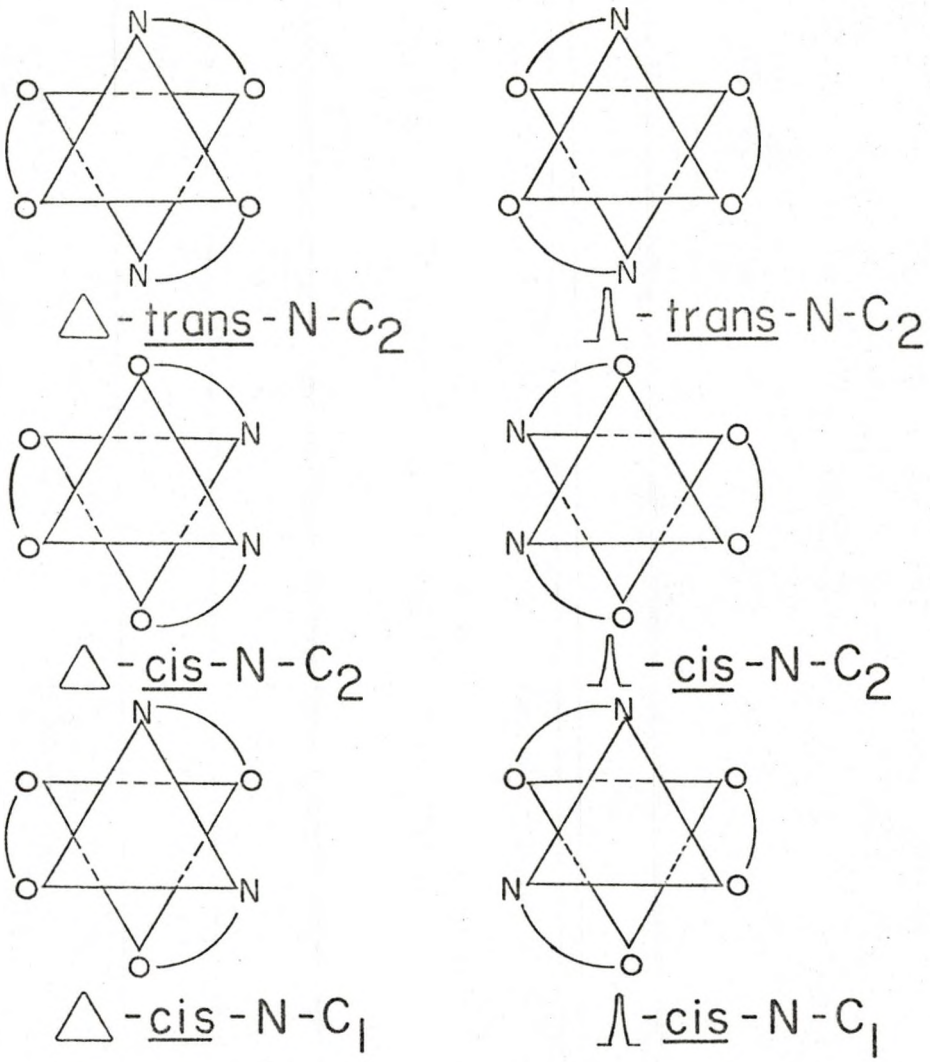


Fig. 9.--Possible isomers of $[Co(acac)(S\text{-}amac)_2]$

finite existence under the conditions used to effect the separation. This usually means solution stability under normal conditions. The method employed to obtain pure stereoisomers of metal complexes is determined by the type of isomers to be separated and the electrical nature of the

complex. Thus it is convenient to discuss ionic complexes and neutral complexes separately.

Ionic complexes

Geometric isomers and diastereomers of ionic tris-chelate complexes have been separated by fractional crystallization from water with careful selection of the proper counter ion. This technique frequently leads to pure samples of the less soluble isomers, however the very soluble isomers are often difficult to isolate and purify.

A more widely utilized technique for separating ionic isomers involves ion exchange chromatography. Many stereochemically complicated systems, both cationic and anionic have been separated by ion exchange resins once the proper eluent salt concentration is discovered. The stereoisomers obtained in this manner are contaminated by unwanted simple salts from the chromatographic eluent unless additional steps are undertaken to remove the impurities.

The separation of a racemate into its enantiomers, a resolution, requires the use of a dissymmetric resolving agent. For ionic complexes the resolution is very frequently accomplished by the use of a dissymmetric counter ion complex. For example, if an ionic tris-chelate racemate, Δ and Λ, is mixed with a half molar amount of the Δ' isomer of another ionic complex with equal and opposite charge, two salts are possible, $\Delta\,\Delta'$ and $\Lambda\,\Delta'$. These salts are

diastereomeric and need not possess the same scalar physical properties. In most cases the $\Lambda\,\Delta^{l}$ diastereomer is less soluble than the other diastereomer and can be removed by fractional crystallization. If the resolving agent can then be effectively removed a successful resolution for both isomers has been accomplished. This technique, however, requires the prior preparation of a series of ionic resolving agents in order to resolve both cationic and anionic complexes.[11]

Neutral complexes

Since neutral tris-chelate complexes exhibit one of two solubility characteristics (vida supra) their separation will be discussed separately. For inner complexes that are only slightly soluble in water and insoluble in non-aqueous solvents, such as tris amino acid complexes, the separation of diastereomers and geometric isomers has been accomplished by fractional crystallization from water.[45] Resolution of this type of complex is difficult and has only been moderately successful with the use of dissymmetric chromatographic substrates such as quartz,[45, 46] and potato starch.[45, 47]

Neutral tris-chelate complexes such as tris-(β -diketonates) that are only soluble in non-polar media have been separated into diastereomers and geometric isomers by the use of alumina and silica adsorption chromatography.[48] Some volatile tris-(β -diketonates) have been separated by gas chromatography.[49] Resolution of this type

of non-polar enantiomer has been moderately successful using chromatographic columns with sugar substrates.[50] However, the complete resolution of uncharged molecules continues to be an underdeveloped area of chemistry.

Determination of the Chirality of Tris-Chelate Complexes

Once a tris-chelate complex is obtained in pure isomeric form its structure may be determined by several techniques. For any description of the geometry, configuration or chelate ring conformations of a complex to be meaningful, however, the structure of the isomer under consideration must remain unchanged for a finite period of time. In other words an energy barrier must exist preventing conversion of that single stereoisomeric form under study, to any other stereoisomeric form or forms for the duration of the experiments required to make the structure determination. The geometry and helical arrangements of many tris-chelate complexes do not change under conditions required for structure determination. However, chelate ring conformations may change very rapidly in solution depending upon temperature.[26]

Absolute configuration by X-ray diffraction methods

Absolute configuration is defined as the exact three dimensional structure of a molecule which requires that the position in space of every atom in the molecule be known relative to all the other atoms.

For metal complexes the only technique that has been successful in determining absolute configuration is single crystal X-ray diffraction. Normal X-ray diffraction methods give rise to bond lengths and bond angles of a molecule, however, in general isomerism other than geometric arrangement cannot be distinguished by this method.[14]

If after a preliminary structure analysis has been done, a second irradiation is performed at a wavelength slightly shorter than the absorption edge of the metal atom, the resulting scattering can be used to distinguish between enantiomers. This method outlined by Bijvoet[51] is not difficult once the initial structure has been determined. Pepinsky and Okaya[52] have described a method applicable to enantiomers without requiring a second irradiation, however, this technique is less sound. If a dissymmetric center of known configuration is incorporated into a molecule, as is often the case in diastereomeric complexes containing an amino acid, the absolute configuration of that molecule can be found by normal X-ray analysis. This crystal engineering method has been applied to a large number of metal complexes.[14] In any case, however, an X-ray structure determination is a major experimental endeavor in terms of time and the cost of equipment.

Configuration relationships by the optical CD method

Tris-chelate complexes exist in the chiral forms, Δ and Λ, which are called the helical configuration or chirality of the complex.

Generally it is only desired to know which chirality is present for a particular isomer and this may be determined empirically by several spectroscopic techniques. Circular dichroism spectroscopy (CD), which measures the effect of ligand dissymmetry on the electronic transitions of the metal d electrons, has been found to be systematically related to the chirality of metal complexes. In order to discuss CD, a brief background concerning the optical properties of molecules is in order.[14, 53]

Molecular asymmetry or dissymmetry has long been denoted as optical activity. The term "Cotton Effect"[14] refers to the unequal absorption of left or right circularly polarized light by an "optically active" chromophore. Monochromatic plane polarized light undergoes a rotation upon passing through an optically active media and this phenomenon is called optical rotary dispersion (ORD). When the rotation is observed at a single wavelength the rotation, α (positive or negative), is reported in terms of specific rotation, $[\alpha]_\lambda$, or molecular rotation, $[M]_\lambda$, for a specific wavelength of visible light.

Specific and molecular rotations are convenient labels for optically active molecules, but they are completely unrelated to molecular structure. However, the unequal absorption of left and right circularly polarized light or CD of an optically active media has been shown to provide stereochemical information. CD spectra are recorded over a range of wavelengths and plotted in terms of molar ellipticity, which is

related to the difference in extinction coefficients of the media for right and left circularly polarized light,[14, 53]

For transition metal complexes the CD absorption in the long wavelength visible region of the metal d-d electronic transition is of interest. For spin paired d^6 cobalt(III) complexes of octahedral symmetry, O_h, the long wavelength visible band has been assigned to the $^1T_{1g} \longleftarrow {}^1A_{1g}$ transition of the metal d electrons. This transition is not optically active, however, because it is electric dipole forbidden even though magnetic dipole allowed. In order to produce an optically active CD band the electronic transition must be both electric dipole allowed (EDA) and magnetic dipole allowed (MDA).

O_h symmetry includes an inversion center and improper axes of rotation and thus would not be expected to show optical activity. By descending in symmetry it is possible to describe complexes that have been studied by CD in terms of their optically active electronic transitions.

In the case of D_3 symmetry for a complex ion such as $[Co(en)_3]^{3+}$ the degeneracy of the $^1T_{1g}$ excited energy level is removed giving rise to $^1A_2$ and ^1E components. The transitions for these component levels are EDA and MDA and thus both produce optically active CD bands. It has been found that Λ-(-)$_D$-$[Co(en)_3]^{3+}$,[13] as identified by X-ray structure determination, exhibits positive $^1E \longleftarrow {}^1A_1$ and negative $^1A_2 \longleftarrow {}^1A_1$ CD transitions. The latter is very weak causing the former

transition to dominate the CD spectra.[54] For complexes of C_3 symmetry such as fac-$[Co(S\text{-}pn)_3]^{3+}$ the situation is very similar with the Λ isomer showing a dominant positive $^1E \longleftarrow {}^1A_1$ transition.[55] Observation of the CD spectrum of complexes like the above whose structure and chirality are known by X-ray methods has led to a general rule. If the major component of the long wavelength CD band is positive the chirality of the complex is Λ.[14, 53] The converse of this rule applies as well.

Complexes that possess C_2 symmetry may also exhibit optical activity, however, the components of their CD spectrum are less well understood. C_2 symmetry causes the parent $^1T_{1g}$ excited energy level to split into three bands all of which are optically active. The bands are $^1A \longleftarrow {}^1A$, $^1B \longleftarrow {}^1A$ and $^1B \longleftarrow {}^1A$ but these are seldom resolvable except for $[Co(mal)_2(en)]^-$,[56] $[Co(EDTA)]^-$[56] and $[Co(S\text{-}glu)_3]$.[57] In these cases the isomers exhibit positive CD bands for the B symmetry levels which dominate the negative CD band of the A symmetry level. Thus the sign of the dominant CD band is considered in making chiral assignments for complexes of C_2 symmetry in which the three bands are unresolved.[14]

The least understood situation is complexes with C_1 symmetry in which the three optically active electronic transitions no longer have their signs determined by symmetry. In practice complexes with C_1 symmetry exhibit two CD bands of opposite sign. Chiral assignments in this case are made by observing the sign of the most intense CD band.

Complexes that have the Λ configuration, as shown by X-ray, also have intense positive CD bands. Therefore an optically active complex with C_1 symmetry exhibiting an intense positive CD band is assigned a Λ helix by this argument.[14, 53]

The sign of the CD absorption band of the d-d transition has been used to assign the configurational relationships of many transition metal complexes, however, there are some limitations to its application. For complexes of C_2 or C_3 symmetry the CD component bands are seldom resolvable and thus use of the "dominant band" method could be misleading if configurational and vicinal effects cause equivalence or even a reversal of band intensities.[14] In the case of C_1 symmetry CD assignments are considered inappropriate by many authors because the electronic transitions are not symmetry determined. For ionic complexes the intensities of the CD bands are affected by ionic strength variations of the solution being measured and the presence of various counter ions of different types. It must then be concluded that the character of the media surrounding an optically active chromophore affects the behavior of CD transitions.[58] Neutral complexes should be well behaved in this connection due to the lack of ions present in solution, assuming that the solvent interaction with neutral complexes is minimal.

Helical configuration
by the exciton method

Another optical method for determining the chirality of certain metal complexes involves the ultraviolet exciton CD band technique as outlined by Bosnich.[19] For complexes containing at least two o-phen, dipy or acac ligands, the coupled long axis polarized $\pi \rightarrow \pi^*$ electronic transitions of the ligands are optically active. The transitions are an order of magnitude more intense than metal d-d transitions and can be related to molecular configuration in a non-empirical manner. For a Λ helix the A_2 transition is left handed, therefore producing a negative CD band at higher energy than the corresponding positive doubly degenerate E transition. Thus by observing the very intense transition in the 30,000 to 40,000 cm^{-1} spectral range, the chirality of a bis- or tris-chelate complex (with π delocalized bidentate ligands) can be determined without reference to a model complex of known configuration. Several iron, ruthenium, silicon and chromium complexes have been assigned by this technique.[18]

Chirality by proton magnetic
resonance methods

Methods to predict the chirality of Δ and Λ diastereomers, but not applicable to enantiomers, involve the use of proton magnetic resonance spectroscopy (pmr). Since diastereomers have different scalar physical properties, the difference in the magnetic environment

of diastereomers can in principle be measured by a pmr experiment when protons are present in the molecule. If this difference in proton chemical shift between the diastereomers can then be systematically related to some structural feature present in complexes of known chirality, a model can be developed.

C-N bond anisotropy

Legg et al.,[59] have reported that the magnetic anisotropic effect of the C-N bond in certain cobalt(III) complexes of EDDA can be related to structure. Their model was based on the idea that certain protons of the EDDA ligand would experience a shielding or deshielding effect depending upon their arrangement with respect to the C-N bonds in the system. The mode of coordination of the ligand to a metal ion was then deduced from the chemical shifts of these protons.

N-D bond steric compression

Dabrowiak and Cooke[20] assigned the chirality of the diastereomers of $[Co(S\text{-amac})(en)_2]^{++}$ complexes using a steric compression argument concerning the relative chemical shifts of the S-amino acid methine hydrogen. Their model states that an amino acid methine proton in line with and sterically crowded by an N-D group of en resonates at lower field than a similar proton above or between the N-D's of coordinated en. The assignments made by this model are consistent with CD results for

the systems studied. This reasoning is applicable only to en complexes and does not consider complexes with ligands having oxygen donor atoms.

C-O bond anisotropic deshielding

Berends and Brushmiller[38, 42] have studied a series of amino acid-cobalt(III) complexes by pmr spectroscopy and proposed the C-O bond magnetic anisotropic deshielding model to predict chirality. For the systems $[Co(N\text{-me-S-ala})_2(ox)]^-$, $[Co(S\text{-ala})(ox)_2]^=$ and $[Co(S\text{-ala})_2(ox)]^-$, chemical shifts of the protons of the S-amino acid ligand were systematically related to the chirality of the diastereomers. The magnetic anisotropic deshielding model states that a proton in line with the C-O bond of an adjacent coordinated ligand would be deshielded relative to a similar proton above the bond.

Stadtherr and Brushmiller[60] applied C-O bond magnetic anisotropic deshielding in assigning the chiral diastereomers of $[Co(ox)_2(R\text{-pn})]^-$ from pmr chemical shifts. The ligand R-pn exhibits a complicated $ABCX_3$ pmr splitting pattern which was solved and bond anisotropy was then applied to the chemical shifts of each of the protons. Only those protons whose position changed relative to the C-O bond of an adjacent ox ligand between the two chiral diastereomers were found to undergo chemical shifts. Thus bond magnetic anisotropy was shown to be useful and predictable for chiral diastereomers and not an unexplainable anisotropy surrounding the entire molecule.

Larson et al.,[61] has also used the magnetic anisotropic deshielding argument in assigning the stereochemistry of the diastereomers of $[Co(ox)_2(N,N'\text{-dimeen})]^-$ using the N-methyl group chemical shifts.

Juhala[62] has shown that the C-O bond deshielding model can be extended to predict the geometry of metal complexes in restricted circumstances. The model was originally intended to assign the chirality of diastereomers only. If, however, the total anisotropy surrounding geometric isomers is very similar as is the case for chiral diastereomers, then the model can be applied. On this basis Juhala was successful in assigning the geometry of a series of Co(III)-NTA complexes containing tfa and ibn.

Recently Everett and Johnson[24] have measured the ^{59}Co nuclear magnetic resonance chemical shifts of a series of chiral tris-chelate cobalt(III) complexes. An attempt was made to relate crystal field orbital splitting energies to the temperature independent paramagnetism of the Co(III) ion. Qualitative explanations of ^{59}Co chemical shifts were found, however, geometric and diastereomeric arrangements were not predictable by this technique.

Statement of the Problem

A series of mixed ligand tris-chelate cobalt(III) complexes will be prepared and separated into their stereoisomeric forms. The isomers will then be used to test the proton magnetic resonance bond anisotropic

deshielding model for assigning chiral complexes. Circular dichroism will be used as a comparative method for the chiral assignments. The systems chosen are $[Co(acac)_2(S\text{-amac})]$ and $[Co(acac)(S\text{-amac})_2]$ for several reasons. These complexes are non-electrolytes (neutral complexes) and thus potentially offer physical properties which will facilitate separating and studying the isomers.

The proton magnetic resonance method has been applied to complexes with ligands containing carboxylate groups (amino acids and di-functional carboxylic acids), however, the systems selected in this study incorporate the ligand acac which contains enolate C-O bonds. Thus if the magnetic deshielding model is correct, the acac ligand should demonstrate the versatility of the model. Also acac contains protons which may be observed in terms of the total magnetic environment of the chiral diastereomeric complexes. This probe of portions of the diastereomers far removed from predictable anisotropies is a critical test of the model.

EXPERIMENTAL

Reagents

All chemicals used were analytical reagent grade unless otherwise specified. Solvents used for chromatography were technical grade and not purified prior to their use.

Preparation of Ligands

The ligands were obtained commercially except N-me-S-ala which was generously donated by V. Kubik and N-me-S-val which was prepared by the method of Quitt et al.[63]

Preparation and Separation of Complexes

Preparation of sodium dinitrobis-(2,4-pentanedionato)cobaltate(III)

Sodium dinitrobis(2,4-pentanedionato)cobaltate(III) was prepared by the method of Boucher and Bailor[64] with slight modifications. A solution containing 35 ml (.32 moles) of technical grade 2,4-pentanedione (acetylacetone) and 12.8 g (.32 moles) of NaOH in 200 ml of distilled water was added to a solution containing 60 g (.148 moles) of sodium hexanitrocobaltate(III) in 200 ml of distilled water. The resulting mixture was stirred mechanically for five minutes, then suction filtered through

filter paper to remove the pink bis(2,4-pentanedionato)cobalt(II) complex. The resulting brownish-red solution was allowed to stand overnight at 5° C whereupon a red solid formed. The red solid was collected by suction filtration on sintered glass and washed with 50 ml of 95% ethanol, 100 ml of acetone to remove the green tris(2,4-pentanedionato)-cobalt(III) complex and air dried. The crude product was dissolved in a minimum amount of distilled water and rapidly suction filtered onto an excess of solid $NaNO_2$, 40 g. The resulting solution was kept at 0° C for fifteen minutes then suction filtered, washed with 95% ethanol, acetone, ether and air dried. The yield was 36.4 g, 65%. The product exhibits the following visible absorption spectra data: λ_{max}, obs., 537 nm, 332 nm; lit., 532 nm, 328 nm.[64]

Preparation of S-aminoacidatobis-(2,4-pentanedionato)cobalt(III)

The preparation of the aminoacidatobis(2,4-pentanedionato)-cobalt(III) complexes was the same for all amino acids studied: sarc, S-ala, S-val, N-me-S-ala, N-me-S-val, S-pro and S-ser. A procedure similar to the one reported by Laurie[37] was utilized except a new technique was used to isolate the products. In a typical reaction, 10.0 g (.033 moles) of sodium dinitrobis(2,4-pentanedionato)cobalt(III) were dissolved in 240 ml of distilled water and 80 ml of methanol which had been heated to 50° C. Then a solution containing .03 moles of the amino acid and 1.6 g (.015 moles) of Na_2CO_3 in 100 ml of distilled water was

prepared and the solutions were combined. The resulting solution was heated to 50° C, 4 g of activated charcoal (Norit A) added and the heterogenous mixture heated at 50° C for 15 minutes with mechanical stirring. The reaction mixture was rapidly cooled in an ice bath then immediately suction filtered through sintered glass to remove the charcoal. The deep blue filtrate was rotary evaporated with reduced pressure to a thick pasty mass to remove as much solvent as possible. During the evaporation the reaction mixture was warmed to no more than 40° with a water bath. At this point 100 ml of absolute ethanol was added to the flask followed by 200 ml of dry acetone to dissolve the product entirely. Then 30 g of chromatographic grade alumina were added to the solution. The mixture was again rotary evaporated with reduced pressure to a dry finely divided solid resembling the original alumina in particle size. In this process the mixture was heated to no more than 40° using a water bath. This procedure prepares the crude reaction mixture for loading onto an alumina chromatographic column.

Chromatographic separation of the diastereomers of aminoacidatobis-(2,4-pentanedionato)cobalt(III)

In each case the diastereomers of aminoacidatobis(2,4-pentanedionato)cobalt(III), where the amino acid is sarc, S-ala, S-val, N-me-S-ala, N-me-S-val, S-pro or S-ser, were separated directly from the crude reaction mixture described in the previous section. A pyrex

chromatographic column; 35 cm in length, 2 cm inside diameter, fitted with a sintered glass filter at the bottom and a ground glass joint at the top was packed with a chloroform slurry of Brockman Activity I alumina (80 to 200 mesh particle size). In each system separated the pH of the alumina (pH = 4.2 to 8.0) was not a critical factor. The column was tapped gently with a padded glass rod while adding the slurry. After the alumina was packed to a height of approximately 20 cm, 100 ml of chloroform was eluted through the column. At this point, one-third of the dry pre-adsorbed reaction mixture was placed on the top of the alumina column followed by 3 cm of banding sand. The desired products in each of the reactions were then obtained from the chromatographic column by elution with the solvents in the order shown in Table 1.

The green complex tris(2,4-pentanedionato)cobalt(III) elutes first from the column and is completely removed from the desired product. By steadily increasing the polarity of the eluting solvent according to the scheme in Table 1, the desired blue complex S-aminoacidatobis-(2,4-pentanedionato)cobalt(III) begins to move down the column. At this point the solvent composition is maintained the same (or only varied slightly) until a good separation of the blue band is observed from the red material remaining at the top of the column. The product was then eluted from the column, collected in fractions and the solvent evaporated with a stream of dried air. Pmr was then used to determine pure fractions of individual diastereomers which could be combined.

TABLE 1

CHROMATOGRAPHY SOLVENT ELUTION SCHEME

Solvents	Ratio by Volume
Chloroform	pure
Chloroform: Ethylacetate	50:1
Chloroform: Ethylacetate	25:1
Chloroform: Ethylacetate	10:1
Chloroform: Ethylacetate	5:1
Chloroform: Ethylacetate	1:1
Ethylacetate	pure
Ethylacetate: Ethanol (95%)	100:1
Ethylacetate: Ethanol	50:1
Ethylacetate: Ethanol	25:1
Ethylacetate: Ethanol	10:1
Ethylacetate: Ethanol	5:1
Ethylacetate: Ethanol	4:1
Ethylacetate: Ethanol	2:1
Ethylacetate: Ethanol	1:1
Ethanol (95%)	pure

Preparation of 2,4-pentanedionato-bis(S-alaninato)cobalt(III)

The complex 2,4-pentanedionatobis(S-alaninato)cobalt(III) was prepared from tris(2,4-pentanedionato)cobalt(III), [Co(acac)$_3$], by a modification of the ligand exchange reaction described by Fugii and Ejiri.[65] The desired product was obtained by first dissolving 10.8 g (0.03 moles) or [Co(acac)$_3$] in 350 ml of hot methanol. Then a solution containing 5.34 g (0.06 moles) of S-ala and 3.60 g (0.06 moles) of KOH in 150 ml of distilled water was added to the green methanol solution. The resulting solution was heated to 60° C and 3 g of activated charcoal (Norit A) was added. The heterogeneous mixture was then stirred mechanically and kept at 60° C for 15 minutes. At this time the reaction mixture was rapidly cooled to room temperature in an ice bath and then suction filtered through sintered glass to remove the charcoal. The highly colored filtrate was rotary evaporated with reduced pressure to a thick pasty mass. A water bath was used to warm the evaporation flask to no more than 40° C during the evaporation of the solvent. In an effort to remove as much water as possible from the products, 100 ml of absolute ethanol and 200 ml of dry acetone were added to completely dissolve the reaction mixture. Then 30 g of chromatographic grade alumina were added to the solution of the products. The mixture was again rotary evaporated with reduced pressure to a finely divided solid resembling the original alumina in particle size. In this process the

mixture was heated to no more than 40° C using a water bath. This procedure prepares the crude reaction mixture for loading onto an alumina chromatographic column.

Chromatographic separation of the stereoisomers of 2,4-pentanedionatobis(S-alaninato)cobalt(III)

The stereoisomers of the complex 2,4-pentanedionatobis(S-alaninato)cobalt(III) were obtained directly from the crude reaction product described in the previous section. An alumina chromatographic column was packed and loaded with the dried sample as was detailed on page 34 of the experimental section. Elution of the complexes was carried out by using the solvent scheme shown in Table 1. Following the removal of the green $[Co(acac)_3]$ and blue $[Co(acac)_2(S\text{-}ala)]$ complexes from the column, continued increase in the polarity of the eluant solvent gives rise to a series of bands on the column. The six bands observed at this point in the procedure were: (in order from bottom to top) large red band, small blue band, large red band, small blue band, large pink band and a small pink band. When all six bands could be seen at one time, the column was equipped with a 1250 ml reservoir of the particular eluant solvent combination which affected this separation. An automatic fraction collector was then employed and elution of the column was carried out using this solvent for 24 hours. After repeated attempts using this procedure, pure samples of the six stereoisomers of this system

were obtained and later identified by pmr spectroscopy. The isomers were labeled A, B, C, D, E and F in the order of elution, Table 4.

Synthesis of tris(2,4-pentanedionato)rhodium(III)

The complex tris(2,4-pentanedionato)rhodium(III) was prepared by a one step, high yield reaction from rhodium trichloride hydrate, $RhCl_3 \cdot 3H_2O$. In a 100 ml round bottom flask equipped with a water cooled condenser, 1.00 g (3.8 mmoles) of $RhCl_3 \cdot 3H_2O$ (Alfa Inorganics) was suspended in 35.0 ml (38 mmoles) of technical grade 2,4-pentanedione(acac). The mixture was heated to 100° C and .65 g (11.6 mmoles) of KOH was added. The reaction mixture was refluxed at 100° C for approximately 20 hours; then the excess ligand was removed by rotary evaporation under reduced pressure. The thick brown material which remained was dissolved in 50 ml of benzene and 5 g of neutral Brockman Activity I alumina (80 to 200 mesh) was added. The mixture was rotary evaporated to dryness under reduced pressure. Column chromatography of the sample on the same alumina and eluting with benzene removes the desired product (first band off the column) from the other reaction products. The yellow-orange complex $[Rh(acac)_3]$ was crystallized from hexane and chloroform, 1:4. The yield was 1.46 g, 88%. The crystalline product gives the following physical data: pmr chemical shifts in $CDCl_3$; obs., methyl singlet (6) 2.10 δ, methine singlet (1)

5.37 δ , lit., 2.10 δ and 5.30 δ ; mp obs., 259 to 259.5° C, lit., 260° C.[66]

Physical Measurements

Electronic absorption spectra

Visible spectra were obtained using a Cary Model 14 spectrophotometer by sweeping from 700 nm to 300 nm. Measurements were made in 1 cm quartz cells using distilled water as a reference. All measurements were made at room temperature (ca 20° C) with no effort made to thermostat the sample.

Rotations

A Rudolph Model 80 high precision polarimeter was used to measure optical rotations. All measurements were obtained in a 1 dm polarimeter tube using the sodium D line (589 nm). Samples were measured in distilled water.

Proton magnetic resonance

The proton magnetic resonance (pmr) spectra were obtained using a Varian A-60 spectrophotometer and were recorded by sweeping from low field to high field. The spectrometer was tuned on the reference signal of the internal standard being used at the time and then returned on the sample. Many different machine settings were used to obtain optimum

spectra, but the R. F. field was always 0.05 mG or less to minimize the possibility of double quantum jumps.

Solutions for pmr spectra were made by dissolving 0.10 to 0.50 g (depending on solubility) of the complex in 0.5 ml of solvent. The samples were run at ca. 40° C, the ambient temperature of the probe.

Sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal reference standard for spectra measured in D_2O and tetramethylsilane (TMS) was used as an internal reference for spectra measured in $CDCl_3$ and acetone-d_6 solvents.

Circular dichroism

The circular dichroism (CD) spectra were obtained on a Cary Model 60 Spectrophotometer in water or chloroform solvent. Dr. G. W. Everett, Jr. of the University of Kansas, Lawrence, Kansas, generously provided the spectra along with his interpretation of the results.

RESULTS AND DISCUSSION

The System $[Co(acac)_2(sarc)]$

Preparation and separation of the diastereomers

The complex $[Co(acac)_2(sarc)]$ was prepared by Laurie's method[37] for synthesizing $[Co(acac)_2(amac)]$ complexes by substituting an equimolar amount of sarc for the amino acid in the procedure. The desired product was isolated and separated into its diastereomeric components directly from the crude reaction mixture by adsorption chromatography on alumina. Elution with ethylacetate first removes the unwanted green $[Co(acac)_3]$ complex from the column. Then a systematic elution with ethylacetate-ethanol solvent mixtures separates the blue complexes of $[Co(acac)_2(sarc)]$ into two components from the remainder of the reaction products. The diastereomers of $[Co(acac)_2(sarc)]$ are soluble in chloroform, acetone and water. No stereoselectivity was observed for this system.

Stereochemistry

The uncoordinated ligand sarc can exist in both the R and S configurations which are rapidly inverting in solution. Upon coordination of the ligand to a metal atom the asymmetric nitrogen atom of sarc

becomes fixed in either the R or S configuration and under certain conditions interconversion of the two forms can be completely eliminated.[67, 68] Incorporation of sarc into the complex $[Co(acac)_2(sarc)]$ has been found to efficiently prevent this inversion of the configuration from occurring as will be demonstrated.

The complex $[Co(acac)_2(sarc)]$ can exist in four stereoisomeric forms similar to the example shown in Figure 4. Two enantiomeric pairs of complexes Δ-R, Λ-S and Δ-S, Λ-R are possible.

Since a diastereomeric relationship exists between these two enantiomeric sets, separation of $[Co(acac)_2(sarc)]$ into two components by non-dissymmetric methods proves that the asymmetric nitrogen atom of sarc has been configurationally fixed by coordination.

PMR of the diastereomers

Chemical shifts for the diastereomers of $[Co(acac)_2(sarc)]$ are given in Table 2. The acac ligand portion of the spectrum for both diastereomic sets show four methyl singlet and two methine singlet resonances as would be predicted for complexes with C_1 symmetry. The first blue band off the column, band A, exhibits an $AMNX_3$ pmr spin-spin splitting pattern for the sarc ligand which is directly analyzable only for the X_3 portion. The second blue band, band B, gives rise to pmr resonances of the sarc ligand similar to band A, but with different chemical shifts. The AMN portion of the $AMNX_3$ pattern shows more

TABLE 2

PMR DATA FOR THE COMPLEXES $[Co(acac)_2(amac)]$

Complex	PMR Chemical Shifts[a]				
	amac			acac	
	Methine	N-methyl	C-methyl	C-methyl	Methine
$[Co(acac)_2(sarc)]$ - A	--[b]	2.08[c]	--[b]	2.02, 2.12 2.22, 2.22[c]	5.50 5.51[c]
$[Co(acac)_2(sarc)]$ - B	--[b]	2.26[c]	--[b]	2.00, 2.12 2.18, 2.20[c]	5.50 5.53[c]
$(+)_D$-$[Co(acac)_2(S\text{-}ala)]$	3.75	--[b]	1.40	1.98, 2.12 2.17, 2.18	5.65 5.66
$(-)_D$-$[Co(acac)_2(S\text{-}ala)]$	3.55	--[b]	1.47	2.00, 2.13 2.15, 2.22	5.66 5.71
$(+)_D$-$[Co(acac)_2(S\text{-}val)]$	3.57	--[b]	0.83 1.10	2.02, 2.12 2.17, 2.20	5.68 5.70
$(-)_D$-$[Co(acac)_2(S\text{-}val)]$	3.40	--[b]	0.91 1.12	2.00, 2.12 2.17, 2.20	5.69 5.72
$(+)_D$-$[Co(acac)_2(N\text{-}me\text{-}S\text{-}ala)]$	3.58	2.24 (2.32)[d]	1.42	2.01, 2.12 2.14, 2.18	5.77 5.78

TABLE 2--Continued

Complex	PMR Chemical Shifts[a]				
	amac			acac	
	Methine	N-methyl	C-methyl	C-methyl	Methine
$(-)_D$-[Co(acac)$_2$(N-me-S-ala)]	3.42	2.01 (2.10)[d]	1.52	2.03, 2.15 2.22, 2.24	5.68 5.75
$(+)_D$-[Co(acac)$_2$(N-me-S-val)]	3.45	2.30 (2.40)[d]	1.10 1.02	2.02, 2.09 2.16, 2.17	5.66 5.67
$(-)_D$-[Co(acac)$_2$(N-me-S-val)]	3.36	2.01 (2.04)[d]	1.06 1.12	2.00, 2.09 2.18, 2.20	5.68 5.71
[Co(acac)$_2$(S-pro)]	--[e]	--[b]	--[b]	2.03, 2.17 2.22, 2.22	5.80 5.80
[Co(acac)$_2$(S-pro)]	--[e]	--[b]	--[b]	2.05, 2.20 2.22, 2.25	5.84 5.90

TABLE 2--Continued

Complex	PMR Chemical Shifts[a]				
	amac			acac	
	Methine	N-methyl	C-methyl	C-methyl	Methine
$[Co(acac)_2(S\text{-}ser)]$	--[e]	--[b]	--[b]	2.03, 2.15 2.18, 2.25	5.78 5.82

[a]Values for the chemical shift are given in ppm from the internal reference DSS in D_2O solvent.

[b]Values are not applicable to this complex.

[c]Values for the chemical shift are given in ppm from the internal reference TMS in $CDCl_3$ solvent.

[d]Values for the chemical shift are given in ppm from the internal reference TMS in acetone-d_6 solvent.

[e]Values were not obtained.

lines in band B than in band A. However, the most striking difference between the pmr spectra of the diastereomeric complexes is that the X_3 N-methyl doublet of band B is centered at 2.26 ppm or downfield 0.18 ppm from the X_3 N-methyl doublet of band A (2.08 ppm).

Application of the PMR method

By inspection of space filling molecular models, the enantiomeric pair Δ-S, Λ-R of $[Co(acac)_2(sarc)]$ places the N-methyl group of sarc directly in line with the C-O bond of an adjacent acac ligand. According to the C-O bond anisotropic arguments mentioned previously,[21, 38, 42] this is a deshielding position relative to the Δ-R, Λ-S enantiomers for the system which place the N-methyl group above an acac C-O bond. Based on this argument the isomers of $[Co(acac)_2(sarc)]$ contained in band B which exhibit the downfield N-methyl group resonance are assigned a racemic mixture of Δ-S and Λ-R enantiomers and band A is assigned as a racemic mixture of Δ-R and Λ-S enantiomers.

Comments on the PMR and CD methods

In this system sets of enantiomers bearing a diastereomeric relationship to each other can be identified and assigned structures by pmr arguments. However, CD spectra of the bands were not measured because racemates are not optically active and therefore cannot exhibit

CD. If, however, the racemates were resolved, CD spectra could be used to make chiral assignments of the enantiomers.[14] This system is a good example of when pmr and CD spectroscopy can and cannot be applied.

The System [Co(acac)$_2$(S-ala)]

In 1969, Laurie reported the synthesis and isolation of a mixture containing the diastereomers of [Co(acac)$_2$(S-ala)].[37] However, no attempt was made to separate the diastereomers and it was suggested that the complex was unstable with respect to disproportionation.

Preparation and separation of the diastereomers

Synthesis of the complex [Co(acac)$_2$(S-ala)] was accomplished using Laurie's technique[37] followed by direct application of the crude reaction mixture to an alumina chromatographic column. Elution with ethylacetate-ethanol solvent mixtures produced the individual blue diastereomers, Δ-S and Λ-S-[Co(acac)$_2$(S-ala)] in pure form. The separation is efficiently monitored by pmr spectroscopy because the diastereomers exhibit different chemical shifts. No stereospecificity was observed, and the diastereomers are soluble in acetone and water and stable to disproportionation for long periods of time (i.e., over six months) in water solution.

Stereochemistry

The stereochemistry of this system is quite simple. The two chiral diastereomers Δ-S, Λ-S as illustrated in Figure 4, possess C_1 symmetry and are closely related to the $[Co(ox)_2(S\text{-ala})]^{2-}$ diastereomers studied by Berends.[38, 42] However, the use of acac instead of ox in a system of this type produces more protons to observe by pmr, thus the symmetry and overall magnetic character of the diastereomers are easily determined.

PMR of the diastereomers

All pmr chemical shifts obtained for the diastereomers of $[Co(acac)_2(S\text{-ala})]$ are given in Table 2. In D_2O solvent $(+)_D$-$[Co(acac)_2$-(S-ala)], which eluted first from the chromatographic column, exhibits a coordinated S-ala methyl group doublet and a methine quartet, after the N-H protons have exchanged for deuterium. The coordinated acac ligands produce four methyl group singlet and two methine singlet resonances as expected for C_1 symmetry. $(-)_D$-$[Co(acac)_2(S\text{-ala})]$, the second isomer off the column, reveals the same pmr splitting pattern and coupling constants, however, the chemical shifts are slightly different. The $(-)_D$ isomer methyl doublet of S-ala is deshielded by 0.07 ppm relative to the $(+)_D$ isomer. The S-ala methine quartet is deshielded in the $(+)_D$ isomer by 0.20 ppm relative to the $(-)_D$ isomer. Thus the $(+)_D$ isomer has a shielded methyl and a deshielded methine relative to the

$(-)_D$ isomer for the coordinated S-ala ligand. The only notable difference for the acac portion of the pmr spectrum between diastereomers is a larger chemical shift for the acac methine protons in the $(-)_D$ isomer.

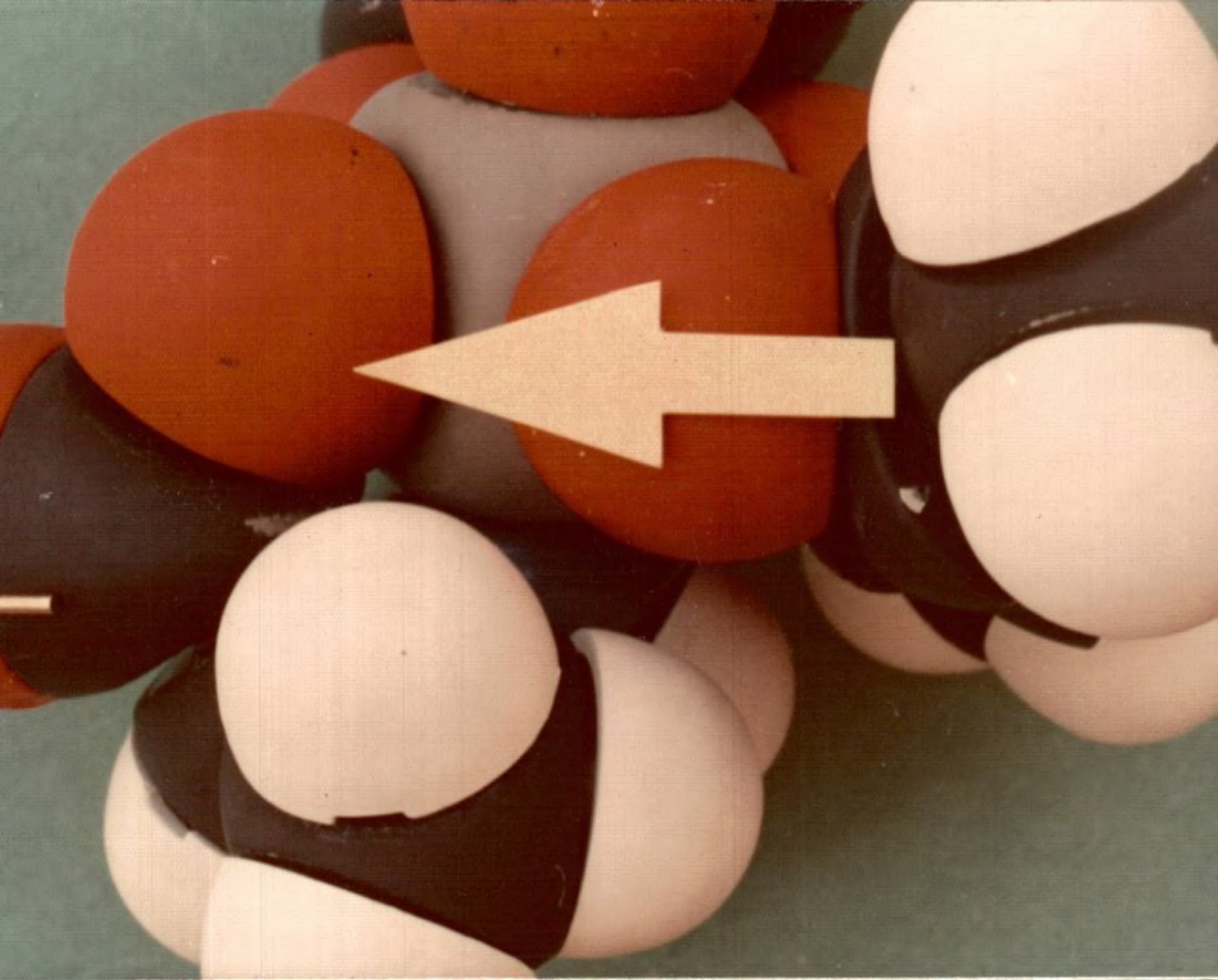
Chiral assignments by the PMR method

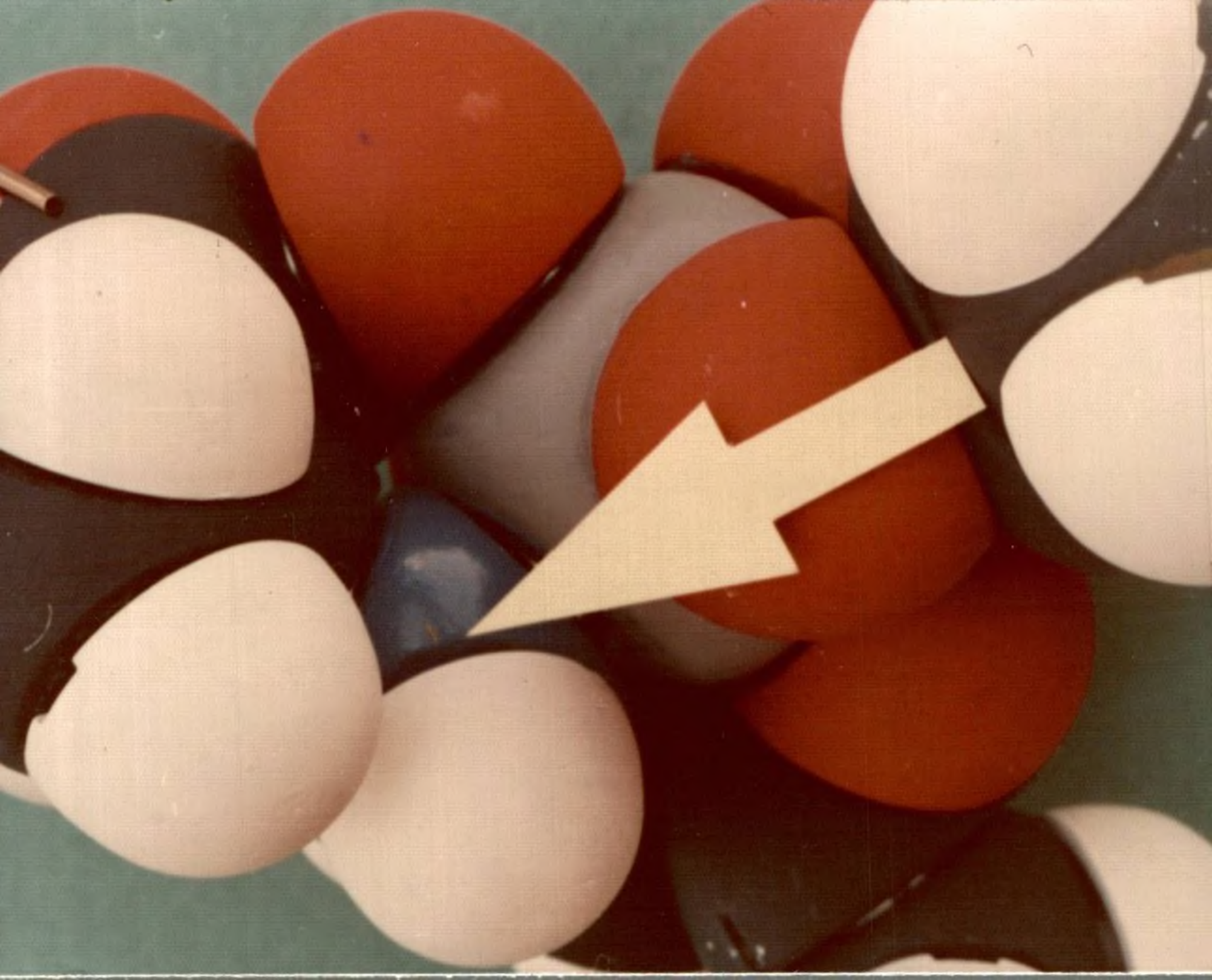
The C-O bond anisotropic deshielding model can be used to predict the chirality of these diastereomers. Analysis of space filling molecular models indicates that a Λ helix for this system places the methyl group of the S-ala above the C-O bond of an adjacent acac ligand as shown in Figure 10. On the other hand the Δ helix places the methyl group of S-ala in line with a C-O bond of acac as shown in Figure 11. The pmr model predicts the Λ isomer to exhibit an S-ala methyl group resonance that is shielded or upfield relative to the Δ isomer.[38, 42]

Figure 12 illustrates that the methine of S-ala in Λ -[$Co(acac)_2$-(S-ala)] is in line with an acac C-O bond. Models also show that Δ -[$Co(acac)_2$(S-ala)], shown in Figure 13, places the methine of S-ala above the C-O bond of acac. According to the pmr model the Λ helix of this system would exhibit a deshielded or downfield methine resonance of S-ala relative to the Δ isomer.[38, 42] Since the $(+)_D$ isomer shows a shielded methyl and a deshielded methine for S-ala relative to the $(-)_D$ isomer, the $(+)_D$ isomer is assigned a Λ helix and the $(-)_D$ isomer is assigned a Δ helix.

Fig. 10.--Methyl group of S-ala in Λ-$[Co(acac)_2(S\text{-}ala)]$ above he C-O bond of an acac ligand.

Fig. 11.--Methyl group of S-ala in Δ-$[Co(acac)_2(S\text{-}ala)]$ in line with a C-O bond of an acac ligand.





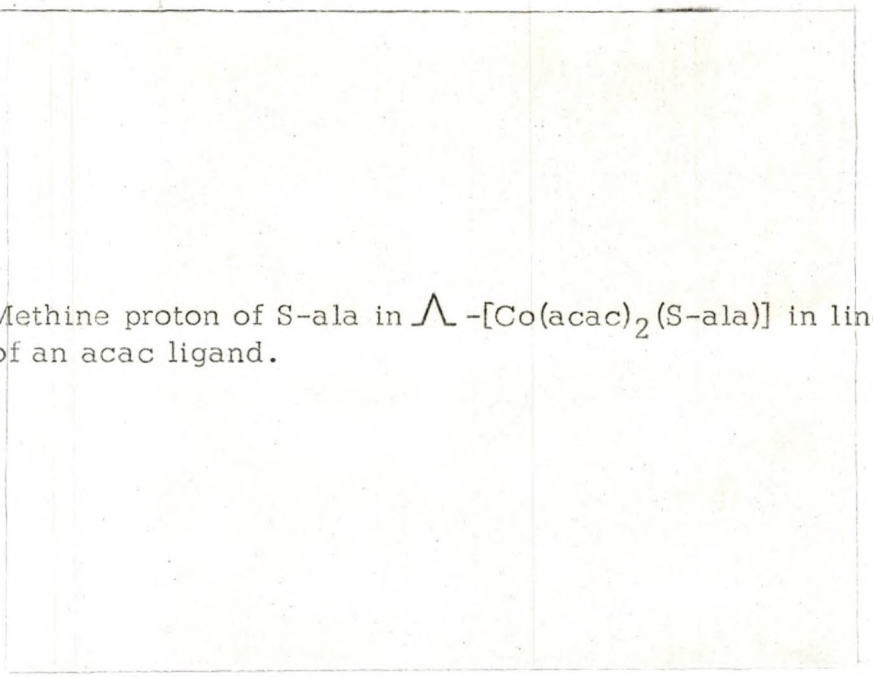
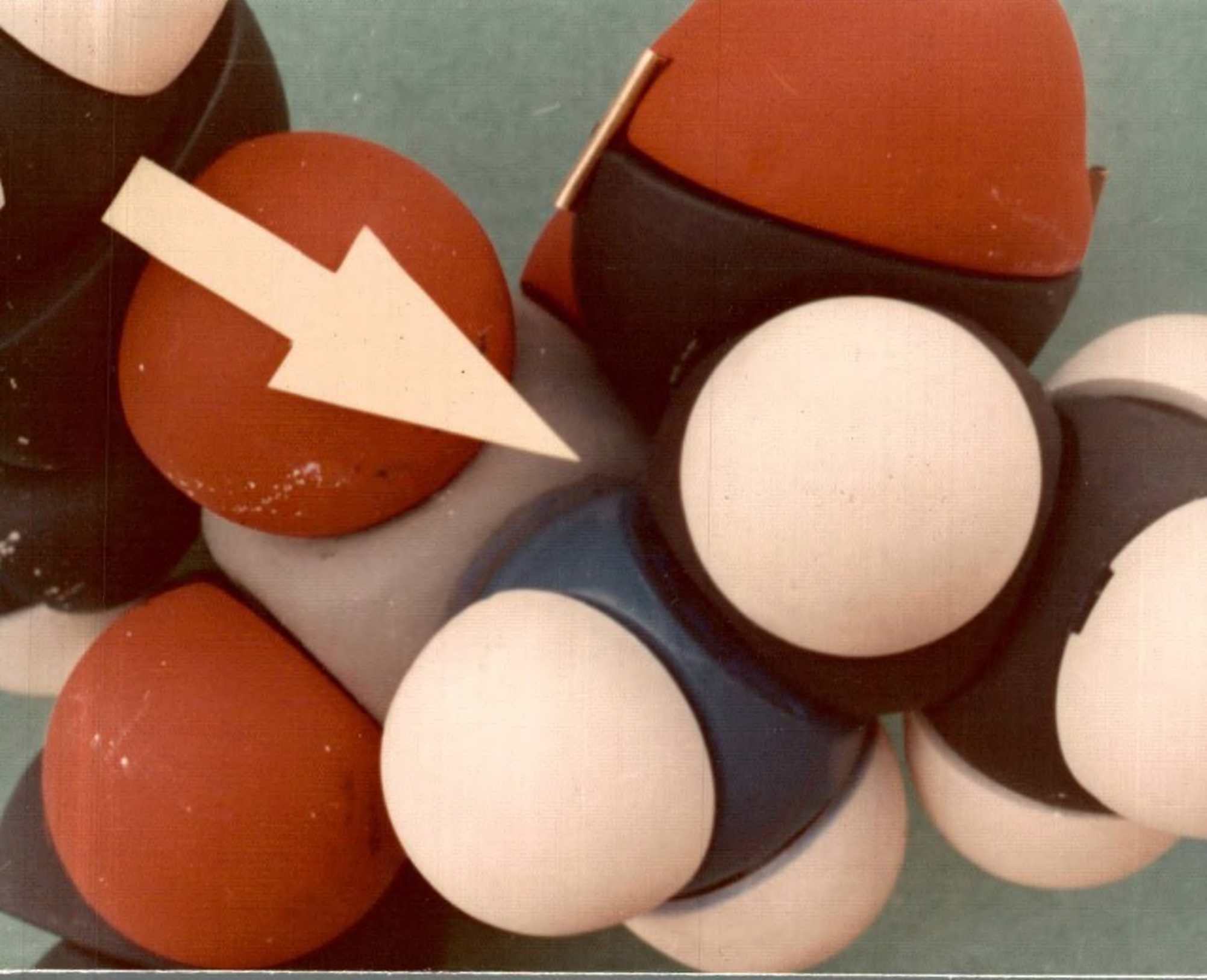
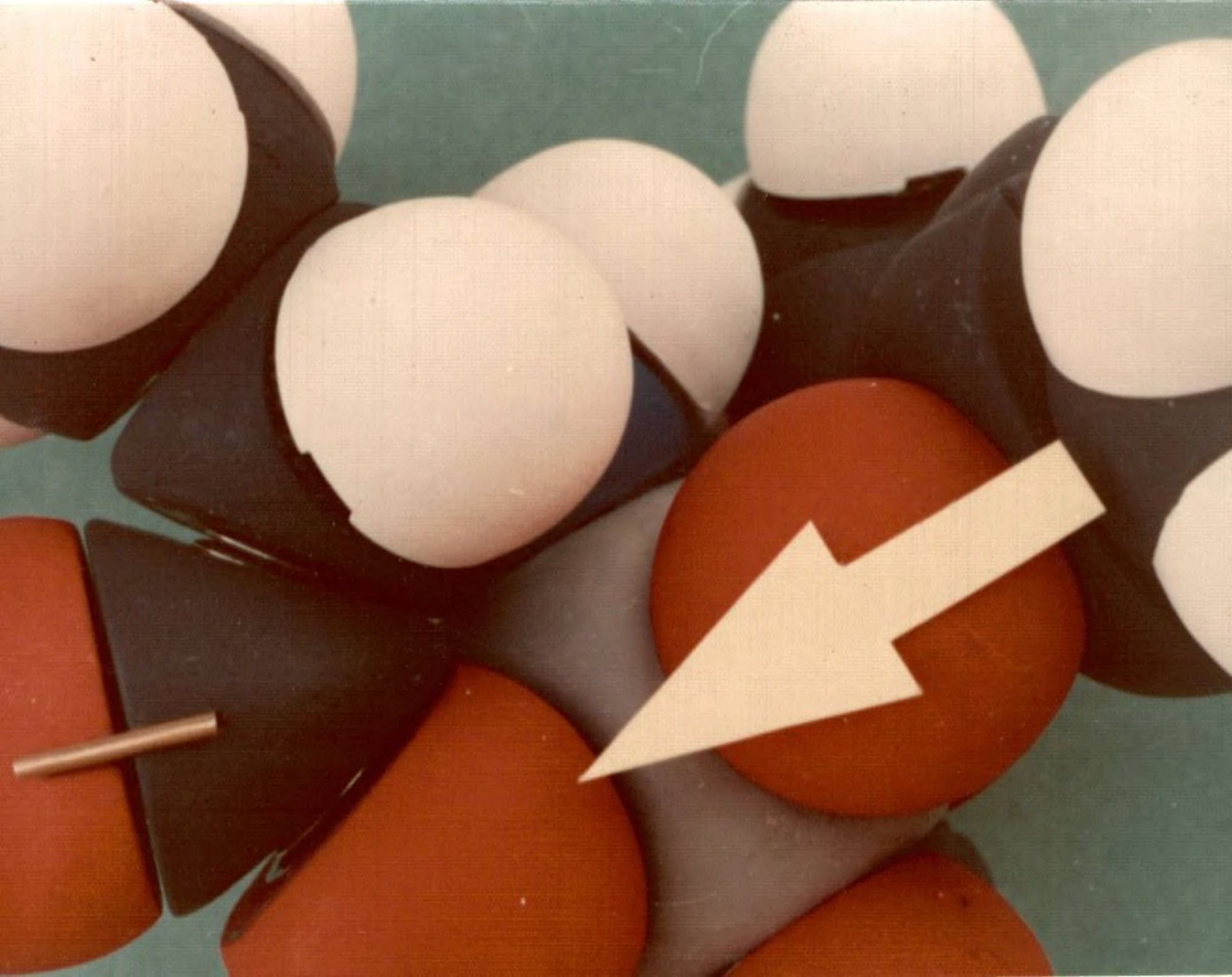


Fig. 12.--Methine proton of S-ala in Λ-[Co(acac)$_2$(S-ala)] in line with a C-O bond of an acac ligand.

Fig. 13.--Methine proton of S-ala in Δ-[Co(acac)$_2$(S-ala)] above the C-O bond of an acac ligand.





Chiral assignments
by the CD method

The visible spectrum long wavelength CD curve of the diastereomers reveals a large positive CD band for the $(+)_D$ isomer indicative of a Λ helix and a large negative CD band for the $(-)_D$ isomer indicative of a Δ helix.[14, 69] Thus CD assignments are in agreement with the pmr assignments which were arrived at by bond magnetic anisotropic deshielding arguments (see Table 3).

The System $[Co(acac)_2(S\text{-val})]$

Preparation and separation
of the diastereomers

The complex $[Co(acac)_2(S\text{-val})]$ was prepared by Laurie's procedure for synthesizing complexes of this type.[37] The crude reaction mixture was chromatographed on an alumina column eluting with ethylacetate-ethanol solvent mixtures (Table 1). Following the removal of the unwanted green $[Co(acac)_3]$ complex, two blue bands were eluted and later identified as being the desired products. The diastereomers were formed in equal amounts in the reaction, no stereospecificity was observed, and the diastereomers are soluble in acetone and water.

Stereochemistry

The complex $[Co(acac)_2(S\text{-val})]$ exhibits the same stereochemistry as the previously described $[Co(acac)_2(S\text{-ala})]$ system. Two diastereomers Δ-S and Λ-S, with C_1 symmetry are possible.

TABLE 3

CHIRAL ASSIGNMENTS BY PMR AND CD FOR THE
$[Co(acac)_2(S\text{-amac})]$ COMPLEXES

Complex	Pmr Assignment	Major Sign of CD Band[a]	CD Assignment
$[Co(acac)_2(sarc)]$ - A	Δ -R, Λ -S	--[b]	--[c]
$[Co(acac)_2(sarc)]$ - B	Δ -S, Λ -R	--[b]	--[c]
$(+)_D$-$[Co(acac)_2(S\text{-ala})]$	Λ	(+)	Λ
$(-)_D$-$[Co(acac)_2(S\text{-ala})]$	Δ	(-)	Δ
$(+)_D$-$[Co(acac)_2(S\text{-val})]$	Λ	(+)	Λ
$(-)_D$-$[Co(acac)_2(S\text{-val})]$	Δ	(-)	Δ
$(+)_D$-$[Co(acac)_2(N\text{-me-S-ala})]$	Λ	(+)	Λ
$(-)_D$-$[Co(acac)_2(N\text{-me-S-ala})]$	Δ	(-)	Δ

TABLE 3--Continued

Complex	Pmr Assignment	Major Sign of CD Band[a]	CD Assignment
$(+)_D$-[Co(acac)$_2$(N-me-S-val)]	Λ	(+)	Λ
$(-)_D$-[Co(acac)$_2$(N-me-S-val)]	Δ	(-)	Δ

[a]Sign indicates the sign of the dominant CD band in the long wavelength region as measured in $CHCl_3$.

[b]CD was not obtained.

[c]Not applicable.

The ligand S-val

Before discussing the pmr spectrum of the diastereomers of $[Co(acac)_2(S\text{-val})]$, the pmr spin-spin splitting pattern for the free amino acid S-val will be mentioned. Figure 14 illustrates the three non-eclipsed rotamers of S-val along the carbon-carbon bond that joins the

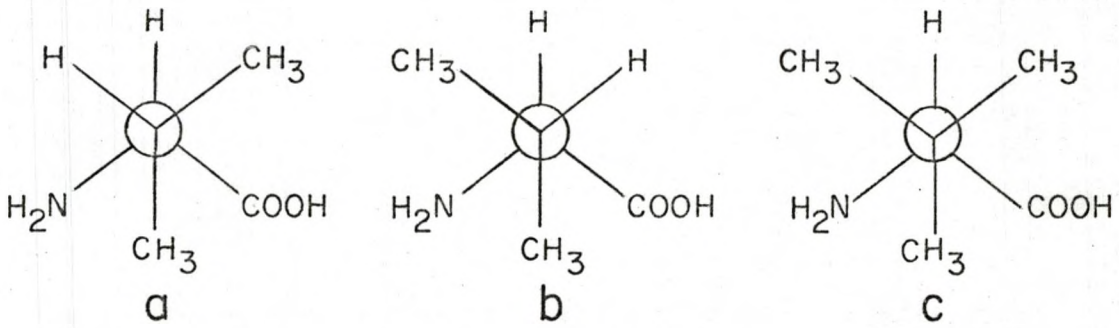


Fig. 14.--Possible rotamers of S-val

isopropyl group to the amino acid chain. Rotation of the isopropyl group about this bond is not hindered and therefore all three rotamers can exist with rotamer c being slightly more favorable than the others from steric considerations. The asymmetric carbon atom provides a magnetic environment that cannot be time averaged by rapid rotation and thus the methyl substituents of the isopropyl group are magnetically non-equivalent. This situation gives rise to an AMX_3Y_3 pmr spin-spin splitting pattern for S-val.[70, 71] Coordination of the S-val anion to a Co(III) ion should not alter this pattern although the chemical shifts are expected to change slightly.[41]

PMR of the diastereomers

The diastereomer, $(+)_D$-[Co(acac)$_2$(S val)], which was eluted first from the chromatographic column, exhibits an asymmetric carbon methine doublet resonance for the coordinated S-val downfield by 0.17 ppm from the corresponding methine proton of $(-)_D$-[Co(acac)$_2$(S-val)]. The methine proton of the substituent isopropyl group appears as a broad unresolvable envelope and the methyl substituents of the isopropyl group appear as two non-equivalent doublets in each of the diastereomers. The acac methyl protons reveal four non-equivalent singlet resonances and the acac methines show two singlet resonances in each diastereomer which is indicative of C_1 symmetry. The acac methine resonances are slightly more separated in the $(-)_D$ diastereomer. All chemical shifts are given in Table 2.

Chiral assignments
by the PMR method

Since S-val and S-ala are configurationally related[28] and differ only in the substituent group on the amino acid, Figures 12 and 13 can be used in discussing the [Co(acac)$_2$(S-val)] system. The asymmetric carbon atom methine of S-val is deshielded by a C-O bond of an adjacent acac ligand in the Λ helix as shown in Figure 12. The situation shown in Figure 13 reveals that a Δ helix places the methine proton above an acac C-O bond in a shielded environment. Thus $(+)_D$-[Co(acac)$_2$(S-val)]

which exhibits a more downfield pmr resonance for the methine proton is assigned a Λ helix and the $(-)_D$ diastereomer is assigned a Δ helix.

Chiral assignments
by the CD method

CD spectra in the visible absorption region shows a positive long wavelength CD band for $(+)_D$-[Co(acac)$_2$(S-val)] indicative of a Λ helix and a negative long wavelength band for $(-)_D$-[Co(acac)$_2$(S-val)] indicative of a Δ helix.[69] Thus the chiral assignments made by the pmr and CD methods are in agreement (see Table 3).

Comments concerning the
PMR of the diastereomers

The chemical shifts of the substituent methyl groups of the S-val moiety for this system are worth noting, Table 2. In Λ-[Co(acac)$_2$-(S-val)] the two non-equivalent methyl doublets are separated by 13 Hertz (Hz) while the separation is 10 Hz in Δ-[Co(acac)$_2$(S-val)]. This 3 Hz greater difference in the Λ helix is just opposite to that observed for the system $[Co(S\text{-val})(en)_2]^{2+}$, where Sargeson finds a 4 Hz greater separation of the S-val methyl doublets for the Δ isomer.[41] This reversal of chemical shift differences for the chiral forms of acac and en systems cannot be related to chiral structures at this time. However, the rotamer population of the isopropyl group of S-val must be different between the two diastereomeric complexes.

Since the methyl resonances of S-ala for the diastereomers of $[Co(acac)_2(S\text{-ala})]$ can be systematically related to chirality (vida supra), it would seem appropriate to consider the average chemical shift of the methyl resonances of S-val for the $[Co(acac)_2(S\text{-val})]$ system. The average chemical shift of the methyl doublets in the Λ isomer is 61.5 Hz and for the Δ isomer the average is 62.0 Hz. These values are the same within experimental error and therefore the magnetic environment surrounding the methyl groups of S-val between chiral diastereomers of $[Co(acac)_2(S\text{-val})]$ appears to be unaffected by bond anisotropy. This observation is not inconsistent with previous results because the distance between the methyl protons of S-val and the acac C-O bond in $[Co(acac)_2(S\text{-val})]$ is considerably larger than the distance between the methyl group of S-ala and the acac C-O bond in $[Co(acac)_2(S\text{-ala})]$. Magnetic anisotropy decreases proportionally to the cube of the distance from its source[72, 73] and apparently the methyl groups of S-val in the diastereomers of $[Co(acac)_2(S\text{-val})]$ are simply too far removed from the adjacent C-O bond of acac to be systematically affected by it.

The System $[Co(acac)_2(N\text{-me-S-ala})]$

Preparation and separation of the diastereomers

The complex $[Co(acac)_2(N\text{-me-S-ala})]$ was prepared by Laurie's method[37] for synthesizing $[Co(acac)_2(amac)]$ complexes. This was done by substituting an equimolar amount of the ligand N-me-S-ala for the

amino acid in the procedure. N-me-S-ala was generously supplied by V. Kubik. The crude reaction mixture was then chromatographed on an alumina column. Elution with ethylacetate first removes the green complex $[Co(acac)_3]$, then systematic elution with ethylacetate-ethanol solvent mixtures, Table 1, removes the desired two blue $[Co(acac)_2$-(N-me-S-ala)] complexes in separate fractions. The $(-)_D$ diastereomer is eluted prior to the $(+)_D$ diastereomer from the column. Pmr was used to monitor the separation and it also showed that the diastereomers were formed in equal amounts in the reaction. The diastereomers are stable to disproportion both in the solid state as well as in solution and are soluble in chloroform, acetone and water.

Stereochemistry

The ligand N-me-S-ala can coordinate to a metal ion in two ways. The configuration at the nitrogen atom of the free ligand rapidly inverts in solution but becomes fixed upon coordination to a metal ion. Thus it is possible for N-me-S-ala to coordinate R,S or S,S if steric interactions are ignored. (The first letter indicates the configuration at the coordinated asymmetric nitrogen atom and the second letter gives the configuration at the asymmetric carbon atom.) Berends[38, 42] and others[74-77] have reported that only R,S coordination is possible for N-me-S-ala because S,S coordination requires vicinal methyl groups be cis on a five membered chelate ring. Allowing R,S coordination only, the complex

$[Co(acac)_2(N\text{-me-S-ala})]$ can exist in two diastereomeric forms, Δ-R,S and Λ-R,S.

PMR of the diastereomers

Pmr chemical shifts for the diastereomers of $[Co(acac)_2(N\text{-me-S-ala})]$ are given in Table 2. The acac portions of the spectra consist of four methyl group singlet and two methine singlet resonances for each diastereomer. This magnetic non-equivalence of the acac ligands is only possible for complexes possessing C_1 symmetry. The ligand N-me-S-ala gives rise to a pmr spin-spin splitting pattern consisting of a methine quartet, a C-methyl doublet and an N-methyl singlet for each diastereomer following deuteration of the N-H group.

In D_2O the N-me-S-ala ligand methine proton resonance for the $(+)_D$ diastereomer is downfield 0.16 ppm relative to the corresponding resonance for the $(-)_D$ isomer. The amino acid C-methyl group of the $(+)_D$ isomer resonates 0.10 ppm upfield relative to the $(-)_D$ isomer. In both D_2O and acetone-d_6 the N-methyl group resonance appears downfield in the $(+)_D$ diastereomer relative to the $(-)_D$ diastereomer.

Chiral assignments
by the PMR method

Values for the chemical shifts of the diastereomers are given in Table 2. Considering the chemical shifts of the amino acid protons, $(+)_D$-$[Co(acac)_2(N\text{-me-S-ala})]$ exhibits a downfield methine resonance

and an upfield C-methyl resonance relative to $(-)_D$-[Co(acac)$_2$(N-me-S-ala)]. This is the same situation that was found for the diastereomers of [Co(acac)$_2$(S-ala)] (vida supra) and thus chiral assignments for both systems can be made by the same pmr deshielding arguments. This is possible because the amino acid asymmetric carbon atom methines and methyl groups exist in the same spatial arrangement in the diastereomers of both systems. On this basis $(+)_D$-[Co(acac)$_2$(N-me-S-ala)] can be assigned the Λ helix and the $(-)_D$ diastereomer is assigned to a Δ helix.

The methyl group of N-me-S-ala coordinated in the R,S configuration is trans to the C methyl substituent and cis to the methine proton of the asymmetric carbon atom. Thus the N-methyl group would be expected to experience the same relatively shielded or deshielded environment as does the methine proton in the same chiral arrangement of the complex. Since the N-methyl group is a substituent on the donor atom of the amino acid chelate ring, it will be situated closer to the adjacent acac C-O bond than is the asymmetric carbon atom methine proton. Therefore the N-methyl group chemical shifts should be another efficient probe of inter-ligand magnetic anisotropic shielding or deshielding between the chiral diastereomers. The arrangement of the N-methyl group of Λ-[Co(acac)$_2$-(N-me-S-ala)] is shown in Figure 15. In this chiral arrangement the N-methyl group is directly in line with the C-O bond of an adjacent acac ligand. This situation for the N-methyl group is predicted to be

deshielding relative to the N-methyl group of Δ -[Co(acac)$_2$(N-me-S-ala)] which is shown in Figure 16. In the Δ diastereomer the N-methyl group is above the C-O bond of an adjacent acac ligand in a relatively shielded environment. As a result the N-methyl group chemical shift in the isomer of this system is predicted to be downfield relative to the isomer.

The chemical shift of the N-methyl group is downfield in $(+)_D$-[Co(acac)$_2$(N-me-S-ala)] by 0.23 ppm in D_2O solvent and by 0.22 ppm in acetone-d_6 relative to the $(-)_D$ diastereomer. Thus the $(+)_D$ isomer is assigned a Λ helix and the $(-)_D$ isomer a Δ helix in agreement with assignments made by considering methine and C-methyl chemical shifts.

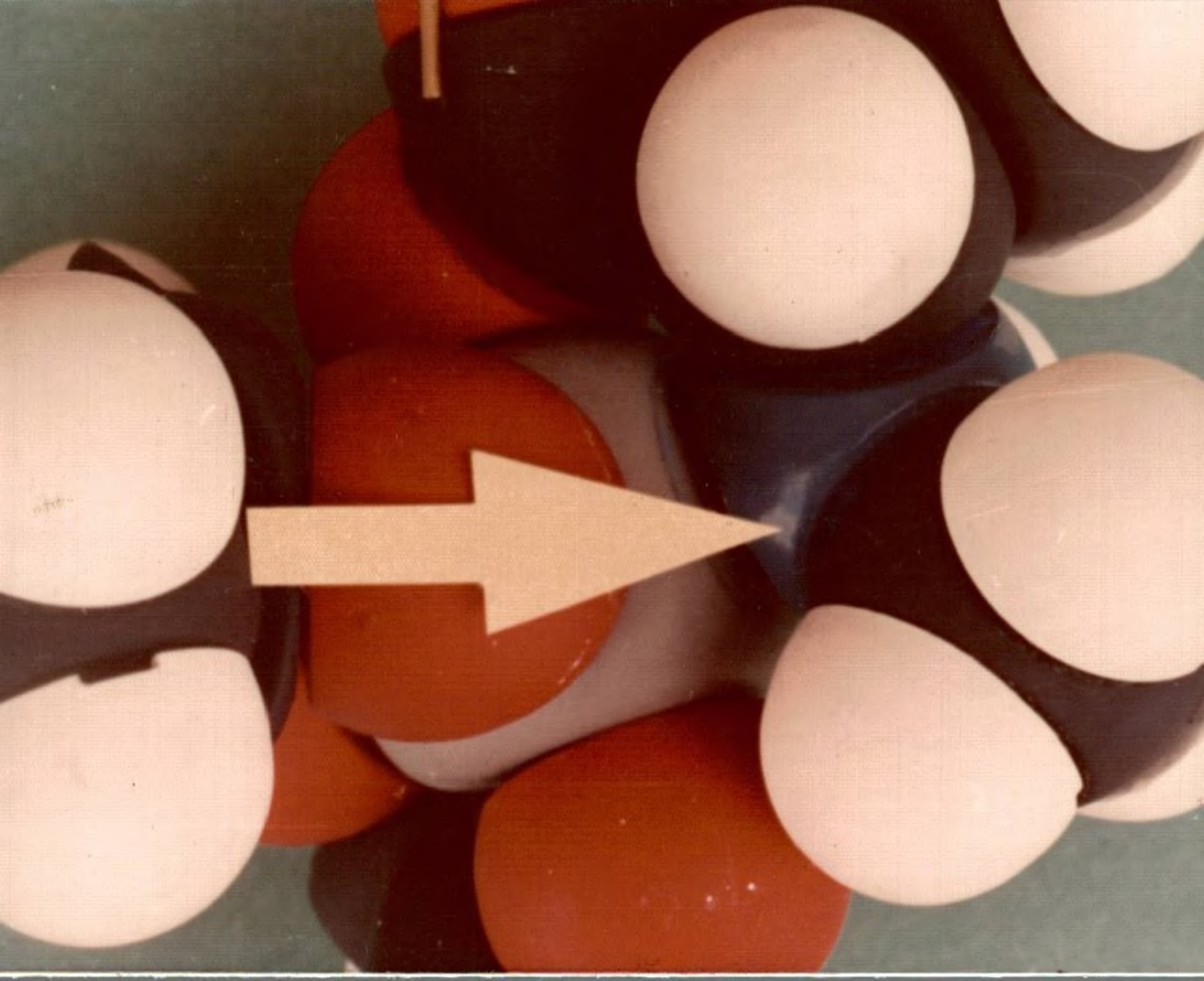
It is important that the chiral assignments made by the pmr method using chemical shifts obtained in either solvent give the same results. This indicates that the relative N-methyl chemical shifts are not solvent dependent but are indeed the result of the chiral structure of the diastereomers.

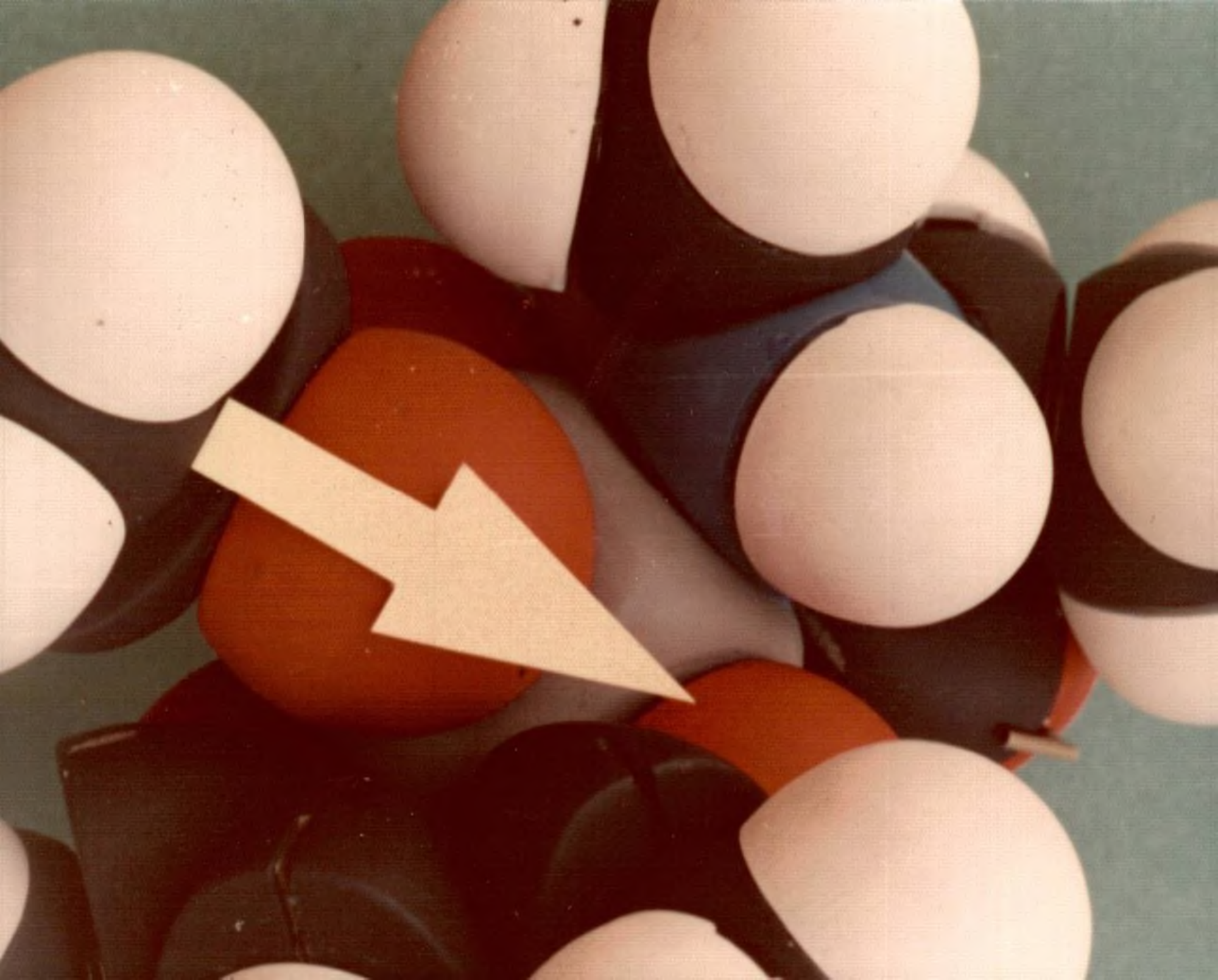
Chiral assignments
by the CD method

The $(+)_D$ diastereomer exhibits a net positive long wavelength CD band indicative of a Λ helix and the $(-)_D$ diastereomer a negative long wavelength CD band indicative of a Δ helix, Table 3. Thus the chiral assignments made by the pmr and CD methods are in agreement.[69]

Fig. 15.--N-methyl group of N-me-S-ala in Λ -[Co(acac)$_2$-N-me-S-ala)] in line with the C-O bond of an acac ligand.

Fig. 16.--N-methyl group of N-me-S-ala in Δ -[Co(acac)$_2$-[N-me-S-ala)] above the C-O bond of an acac ligand.





The System [Co(acac)$_2$(N-me-S-val)]

Preparation and separation of the diastereomers

The complex [Co(acac)$_2$(N-me-S-val)] was obtained using Laurie's[37] method for preparing [Co(acac)$_2$(amac)] complexes. This was accomplished by substituting an equimolar amount of N-me-S-val, which was prepared by the method of Quitt et al.,[63] for the amino acid in Laurie's procedure. Direct application of the crude reaction mixture to an alumina chromatographic column and elution with ethylacetate removes the unwanted green [Co(acac)$_3$] complex followed by the appearance of two blue bands of equal height on the column. Elution of the blue bands from the column with ethylacetate-ethanol mixtures and subsequent identification reveals that $(+)_D$-[Co(acac)$_2$(N-me-S-val)] is eluted first followed by the $(-)_D$ form. No stereospecificity was observed and the diastereomers are soluble in chloroform, acetone and water.

Stereochemistry

The ligand N-me-S-val is predicted to coordinate to a metal ion stereospecifically in the R,S configuration. (The first letter refers to the configuration at the coordinated asymmetric nitrogen atom and the second letter refers to the configuration at the asymmetric carbon atom.) This is a logical conclusion based upon the fact that N-me-S-ala has been found to coordinate exclusively in the R,S form.[38, 42, 74, 75] The isopropyl group of N-me-S-val is expected to offer at least as much steric

interference to a vicinal cis S-N-methyl group upon coordination of the N-me-S-val ligand as does the C-methyl group in the case of coordinated N-me-S-ala. Isolation of two diastereomers for the complex $[Co(acac)_2(N\text{-me-S-val})]$ can be used to support this contention. If both S,S and R,S coordination of N-me-S-val were possible, the complex $[Co(acac)_2(N\text{-me-S-val})]$ could exist in four diastereomeric forms: Δ-R,S, Λ-R,S, Δ-S,S and Λ-S,S. However, only two diastereomers were found and since the uncrowded R,S configuration is expected, it is concluded that S,S coordination of the ligand is eliminated. The two blue complexes eluted from the chromatographic column must therefore be the chiral diastereomers Δ-R,S and Λ-R,S.

PMR of the diastereomers

Pmr data for the diastereomers of $[Co(acac)_2(N\text{-me-S-val})]$ are presented in Table 2. The acac portions of the spectra consist of four methyl group singlet and two methine singlet resonances for both diastereomers. This magnetic non-equivalence of the acac ligands in each case reveals that the diastereomers possess C_1 symmetry.

The spin-spin splitting pattern for the N-me-S-val ligands is the same as found for S-val in the diastereomers of $[Co(acac)_2(S\text{-val})]$ with the addition of the N-methyl group resonances. The methine proton of the asymmetric carbon atom resonates downfield in $(+)_D$-$[Co(acac)_2$-(N-me-S-val) relative to the $(-)_D$ diastereomer in D_2O solvent. The N-methyl group resonates downfield in the $(+)_D$ isomer relative to the

$(-)_D$ isomer in both D_2O and acetone-d_6 solvents. This solvent independence of the relative N-methyl group chemical shift between the chiral diastereomers is important if structural assignments are to be made from pmr spectra.[62]

The methyl substituents of the isopropyl group of N-me-S-val are magnetically non-equivalent in both diastereomers as was the case for the complex [Co(acac)$_2$(S-val)] (vida supra). For $(-)_D$-[Co(acac)$_2$-(N-me-S-val)] the C-methyl doublets are separated by 4.0 Hz and in the $(+)_D$ diastereomers the separation is 1.5 Hz. From this it is possible to conclude that rotation of the isopropyl group is slightly less rapid in the $(-)_D$ isomer relative to the $(+)_D$ isomer.[70, 71] However, since the average chemical shifts of the methyl substituents are the same for both diastereomers, no significant difference in the magnetic environment surrounding the isopropyl group is revealed between the two chiral arrangements.

Chiral assignments
by the PMR method

Arguments presented previously for the system [Co(acac)$_2$(S-val)] may be applied to the pmr chemical shifts of the diastereomers of [Co(acac)$_2$(N-me-S-val)]. For these systems a Λ helix is predicted to exhibit an asymmetric carbon atom methine proton resonance deshielded relative to a Δ helix. On this basis $(+)_D$-[Co(acac)$_2$(N-me-S-val)], with the downfield methine proton resonance, is assigned a Λ helix

and the $(-)_D$ form is assigned a Δ helix. The predicted magnetic environment of the R-N-methyl group was discussed previously for chiral diastereomers of the analogous system $[Co(acac)_2(N\text{-me-S-ala})]$. A Λ helix is expected to exhibit an N-methyl group resonance deshielded relative to a Δ helix and thus $(+)_D$-$[Co(acac)_2(N\text{-me-S-val})]$ with the downfield N-methyl group resonance is assigned a Λ helix and the $(-)_D$ isomer is assigned a Δ helix in agreement with the above predictions.

Chiral assignments
by the CD method

The intense visible long wavelength CD band for $(+)_D$-$[Co(acac)_2$-$(N\text{-me-S-val})]$ is positive indicating a Λ helix and is negative for $(-)_D$-$[Co(acac)_2(N\text{-me-S-val})]$ indicating a Δ helix, Table 3. Thus the chiral assignments made by pmr arguments and the CD method are in agreement.[69]

The Systems $[Co(acac)_2(S\text{-pro})]$ and $[Co(acac)_2(S\text{-ser})]$

Stereochemical considerations

For the systems discussed previously $[Co(acac)_2(S\text{-amac})]$, where the S-amac is S-ala, S-val, N-me-S-ala and N-me-S-val, no preference was found for the formation of one chiral diastereomer at the expense of the other. This lack of stereospecificity is an unexpected result, particularly in the case of S-val[41] and the N-methyl amino acids[38, 42, 74-76]

in which substituent R groups are large enough to cause steric interactions of the amino acid with adjacent acac ligands. On the other hand the very similar complex $[Co(N\text{-me-S-ala})(ox)_2]^-$ has been shown to exhibit a 3:1, Λ to Δ product ratio.[78] Kubik and Brushmiller interpreted this stereospecificity to result from the N-methyl group in the Δ helix being crowded with an adjacent ox ligand. The ox ligand forms a planar five member chelate ring while acac forms a planar six member ring[27] and this difference in ring size may explain the lack of stereospecificity encountered for acac systems. However, acac contains pi delocalized electrons as does ox, and therefore coordinated acac also should be capable of steric repulsion toward groups very near the top or bottom of the chelate ring. This steric hindrance above the ring should be greater than the repulsion for groups approaching the plane of the acac ring for these systems.

The ligand S-pro

In an effort to introduce a stereospecificity resulting from nonbonded interchelate ring steric crowding for acac complexes, the ligand S-pro was selected. S-pro is shown coordinated to a metal ion in Figure 17. The substituent five member pyrrolidine ring causes the nitrogen atom of S-pro to coordinate exclusively in the S configuration.[75, 77, 79] This is obvious when one considers coordinated S-pro gives rise to two fused five member rings. The three methylene groups

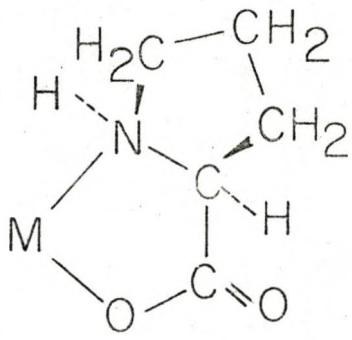


Fig. 17.--Coordinated form of the S,S-proline ligand

forming the pyrrolidine ring must be connected to the amino acid through bonds arranged cis on the chelate ring. Thus for S configuration at the asymmetric carbon atom, the asymmetric nitrogen atom must coordinate in the S configuration.[28] The rigid structure of S,S-pro should test interchelate ring steric crowding between the chiral diastereomers of the complex $[Co(acac)_2(S,S\text{-pro})]$.

Preparation and separation of the diastereomers

The complex $[Co(acac)_2(S,S\text{-pro})]$ was prepared by a ligand exchange reaction utilizing $[Co(acac)_3]$ and the anion of S-pro in aqueous methanol solvent. Activated charcoal was used as a catalyst for the reaction. Column chromatography of the crude reaction mixture effectively removes the green unreacted starting material $[Co(acac)_3]$ from the desired product. Further elution with ethylacetate-ethanol solvent mixtures, Table 1, gives rise to two blue bands of equal height

on the column. By slowly increasing the ethanol content of the eluting solvent, two blue bands are removed from the column in separate fractions and were subsequently shown to be the individual diastereomers of the complex $[Co(acac)_2(S,S\text{-pro})]$.

PMR of the diastereomers

The diastereomers of $[Co(acac)_2(S\text{-pro})]$ exhibit pmr spectra indicative of C_1 symmetry, Table 2. In each diastereomer four acac methyl singlet and two acac methine singlet resonances are found but no significant chemical shifts for the protons are observed between the isomers. The S-pro ligand gives rise to a very complicated pmr spin-spin splitting pattern which is not directly analyzable for individual proton chemical shifts. Thus chiral assignments for the diastereomers of this system have not been made by pmr deshielding arguments.

Stereospecificity of $[Co(acac)_2(S\text{-pro})]$

Since the chiral diastereomers of the system $[Co(acac)_2(S\text{-pro})]$ are formed in equal amounts, no stereospecificity resulting from steric crowding has been demonstrated for acac complexes. It is surprising that even very bulky ligands such as S-pro are incapable of causing crowding with the adjacent acac ligands. Other types of ligands that can impart stereospecificity must be employed, if a model for predicting chirality from isomer abundance is to be developed for complexes of this type.

The ligand S-serine

Hall and Douglas[40] have reported that the ligand S-ser imparts a stereospecificity on the system $[Co(S\text{-}ser)(en)_2]^{++}$. It was postulated that the functional group side chain, R--CH_2OH of S-ser, was involved in a three point attachment[79] which serves to stabilize the Λ helix of the system. A hydrogen bond interaction of the hydroxyl group with the N-H protons of adjacent en ligands is possible only in the Λ form of the complex. By this argument, Λ -$[Co(S\text{-}ser)(en)_2]^{++}$ was presumed to be thermodynamically more stable than the Δ isomer for the system.[33] Hidaka et al.,[43] isolated and assigned the structures of the chiral diastereomers for the system $[Co(ox)_2(S\text{-}ser)]^{=}$, however, the isomer ratio was not reported. Therefore it is not known whether or not S-ser causes stereospecificity in ox systems.

It was felt that preparation of the system $[Co(acac)_2(S\text{-}ser)]$ in the presence of charcoal, which acts as a catalyst for equilibrating Co(III) complexes,[80] would serve to test the stereospecificity of S-ser in diketonate complexes. The diastereomer Δ -$[Co(acac)_2(S\text{-}ser)]$ could be stabilized by a hydrogen bond attachment of the S-ser ligand to the oxygen donor atom of an adjacent acac ligand.

Preparation of the Complex $[Co(acac)_2(S\text{-}ser)]$

The complex $[Co(acac)_2(S\text{-}ser)]$ was prepared by ligand exchange with $[Co(acac)_3]$ and neutralized S-ser in aqueous methanol solvent.

Activated charcoal was added to catalytize the reaction. The crude reaction products were chromatographed on an alumina column eluting with ethylacetate and ethanol solvent mixtures, Table 1. Unreacted $[Co(acac)_3]$ was first eluted from the column followed by a single blue band which was the desired complex. The blue complex $[Co(acac)_2(S\text{-ser})]$ was chromatographed again on alumina with no evidence of diastereomer separation. Fractionation of the eluent from the column followed by pmr spectroscopy revealed that all fractions contained the same material.

PMR of the complex

Pmr spectra in D_2O solvent shows the complex $[Co(acac)_2(S\text{-ser})]$ exhibits four methyl singlets and a slightly broadened methine resonance region for the protons of the acac ligands. Chemical shifts are given in Table 2. The non-equivalence of the acac methyl groups indicate C_1 symmetry and also suggests that only a single diastereomer is present. The S-ser portion of the complex exhibits an ABC pattern that is not easily solved for individual proton chemical shifts. This is to be expected since S-ser contains a methylene group adjacent to an asymmetric carbon atom.[83] Since the chemical shifts of the S-ser asymmetric carbon atom methine protons were not obtained for the two possible helical forms of the complex, chiral assignments by pmr are not possible.

CD spectra of the complex

The visible absorption CD spectra of [Co(acac)$_2$(S-ser)], obtained from Dr. G. W. Everett at the University of Kansas, reveals only a slight optical activity for the complex. This observation is unlike that found for the previously described [Co(acac)$_2$(S-amac)] complexes[69] and probably results from having a mixture of two chiral diastereomers. The vicinal effects of the S-ser ligand could be responsible for the small non-zero CD curve of the complex.[17]

Stereospecificity of S-serine in acac complexes

Conflicting observations by pmr and CD spectroscopy for the complex [Co(acac)$_2$(S-ser)] serve to illustrate a misleading case of near magnetic degeneracy for the acac methyl protons of two diastereomeric complexes. Pmr line counting of the 60 Megahertz (MHz) spectrum of [Co(acac)$_2$(S-ser)] would predict the presence of only a single diastereomer possessing C_1 symmetry, while CD indicates the presence of a mixture of two chiral isomers.

It is sound reasoning that a mixture of diastereomeric molecules is present if certain protons in the sample exhibit non-equivalent chemical shifts, however, the assumption that diastereomers or even geometric isomers must reveal unlike pmr spectra can lead to false conclusions.[81]

A similar situation for the complex [Co(acac)$_2$(2S,3R-thr)] has been found by Wingert.[82] While the 60 MHz pmr spectrum of this complex

indicates the formation of only a single diastereomer, 100 MHz spectra proves that near magnetic degeneracy of the acac protons has occurred between the chiral diastereomers. Direct proof that the sample contained an equimolar mixture of the two diastereomers was provided by observing chemical shifts and coupling constants at different pmr field strengths. The two doublets revealed by the 60 MHz spectrum for the chelate ring methine proton of coordinated 2S,3R-thr could have arisen from trans N-H coupling to the methine proton for a single chiral diastereomer. However, pmr spectra at 100 MHz reveals the presence of two unlike methine protons since the chemical shift between the doublets is field dependent.[83] This is an excellent example of the value of pmr spectroscopy at different magnetic field strengths.

By analogy, the complex $[Co(acac)_2(S\text{-ser})]$ is expected to behave much like $[Co(acac)_2(2S,3R\text{-thr})]$ since both systems contain hydroxl functional group amino acids. Therefore it is concluded that S-ser does not impart a stereospecificity by some hydrogen bond mechanisms to the complex $[Co(acac)_2(S\text{-ser})]$.

The $[Co(acac)(S\text{-ala})_2]$ System

Stereochemistry

Six stereoisomers are possible for the complex $[Co(acac)(S\text{-ala})_2]$ and these are shown in Figure 9. The isomers are Δ and Λ-trans-N-C_2, Δ and Λ-cis-N-C_2 and Δ and Λ-cis-N-C_1, as shown

previously in Figure 9. On a statistical basis the product ratio is expected to be 25% trans-N-C_2, 25% cis-N-C_2 and 50% cis-N-C_1 with a 50:50, Δ to Λ probability within each set of geometric isomers. This prediction does not take into consideration any non-bonded steric interactions between the ligands. However, analysis of space filling molecular models reveals no serious steric crowding exists that would prohibit the formation of any of the isomers. Thus the formation of all six possible stereoisomers is to be expected as Berends found for the similar system $[Co(ox)(S\text{-ala})_2]^{=}$.[38, 42]

Preparation and separation of the isomers

Fujii and Ejiri[65] have reported the preparation and identification of one isomer for the complex $[Co(acac)(S\text{-ala})_2]$. Their method involved a ligand exchange reaction of $[Co(acac)_3]$ and neutralized S-ala in aqueous methanol solvent with activated charcoal as a catalyst. The complex reported was isolated by fractional crystallization.

In this work the method of Fujii and Ejiri[65] was used to prepare the complex $[Co(acac)(S\text{-ala})_2]$, however, an alumina chromatographic column was employed in separating the components of the crude reaction mixture. Elution of the complexes was carried out with a series of binary solvent mixtures using chloroform, ethylacetate and ethanol by slowly increasing the eluting strength of the solvent, Table 1. The green starting material $[Co(acac)_3]$ is first removed from the column followed by the

blue diastereomers of $[Co(acac)_2(S\text{-ala})]$ as described previously. With steadily increasing amounts of ethanol in the eluting solvent a series of six red, blue and pink bands appear on the column. Following several chromatographic runs pure samples of each of the stereoisomers were obtained. The isomers are labeled A through F (see Table 4) in the order of elution (A being eluted first). Several bands remain at the top of the column which comprise the well characterized $[Co(S\text{-ala})_3]$ system.[45, 84]

A systematic approach to structural assignments of the isomers

Since the six stereoisomers of the system $[Co(acac)(S\text{-ala})_2]$ exist as diastereomers and geometric isomers, a step by step analysis is required in order to make structural assignments. Pmr line counting can be used to classify the symmetry of the isomers,[85] therefore necessarily revealing the geometry for the C_1 symmetry case. Visible absorption spectroscopy should then distinguish the trans-N isomers from the cis-N isomers for the remaining C_2 symmetry complexes.[32] Only after the isomers are paired according to geometry can pmr bond anisotropic deshielding arguments be applied to make chiral assignments.[62] In theory CD can be used to assign the chirality of each of the isomers without reference to geometric pairs.

TABLE 4

SPECTRAL DATA, SYMMETRY AND GEOMETRY FOR THE COMPLEXES [Co(acac)(S-ala)$_2$]

Isomer[b]	Visible Absorption Max.[c]	Pmr Chemical Shifts[a]				Symmetry	Geometry
		S-ala		acac			
		Methine	Methyl	Methine	Methyl		
A	524	3.77	1.57	5.75	2.05	C_2	trans
B	570	3.87	1.44	5.83	2.24	C_2	cis
C	524	3.91	1.51	5.74	2.04	C_2	trans
D	570	3.76	1.54	5.85	2.27	C_2	cis
E	532	3.52 3.70	1.39 1.51	5.80	2.05 2.27	C_1	cis
F	533	3.66 3.81	1.40 1.47	5.78	2.05 2.28	C_1	cis

[a]Values for the chemical shifts are given in ppm from the internal reference DSS in D_2O solvent.

[b]Isomers are listed in the order of elution from the chromatographic column with isomer A being eluted first.

[c]Visible absorption maxima are given in nanometers (nm) from spectra obtained in water solvent.

Classification of the isomers of $[Co(acac)(S\text{-}ala)_2]$ by symmetry

Pmr chemical shifts in D_2O for the six isomers of $[Co(acac)(S\text{-}ala)_2]$ are given in Table 4. For the isomers with C_2 symmetry the two S-ala ligands are interchanged by the C_2 rotation axis and are therefore chemically and magnetically equivalent. The methyl groups of the acac ligand for the C_2 isomers are also chemically and magnetically equivalent as a result of the C_2 symmetry. The acac methine proton singlet resonance appears downfield from the other protons in these complexes and ultimately proves very useful in observing the presence of a pure C_1 isomer.

Isomers E and F from the alumina column each exhibit two non-equivalent S-ala pmr spectra consisting of two methyl doublet and two methine quartet resonances. Also two magnetically non-equivalent acac methyl singlets are observed along with a single acac methine peak. Bands E and F can each be shown to be a pure C_1 isomer and not an equimolar mixture of two C_2 isomers by the single acac methine resonance. An equimolar mixture of two C_2 isomers would be expected to produce nearly the same pmr pattern as would a single C_1 isomer were it not for the methine of the acac ligand. However, two C_2 isomers are expected to exhibit individual non-equivalent methine acac singlet resonances, while a C_1 isomer can have only a single acac methine

resonance. Utilizing this argument bands E and F each with a single acac methine resonance are assigned C_1 symmetry.

The first four bands, A, B, C and D were each found to exhibit a single S-ala pmr spectrum consisting of a methyl doublet and a methine quartet resonance. Each isomer also exhibits an acac methyl singlet and an acac methine singlet resonance. Only a complex possessing C_2 symmetry for $[Co(acac)(S\text{-}ala)_2]$ could produce this pmr spectrum in which the integrated acac and S-ala methyl regions are of equal area. Thus bands A, B, C and D are assigned C_2 symmetry, as shown in Table 4.

Geometry assignments

In the above symmetry classification, isomers E and F of $[Co(acac)(S\text{-}ala)_2]$ were found to have C_1 symmetry which is only possible for the cis-N-C_1 geometric arrangement (see Figure 9). For the remaining C_2 isomers, A, B, C and D, it is first required to match geometries or in other words find out which isomers constitute a chiral diastereomeric pair before geometries may be assigned.

Idealized symmetry, which considers only the donor atom arrangement about metal atom, would predict that the two trans-N diastereomers absorb visible light at very nearly the same wavelength.[32] This is also true for the cis-N arrangement. An exception to this rule was reported by Wingert et al.[44] Values obtained from the visible absorption spectra

of the C_2 isomers are given in Table 4. The visible absorption maxima for isomers A and C at 524 nm, and maxima for B and D at 570 nm, are interpreted to mean A and C have the same geometry as do B and D.

Chemical shifts for the acac methyl resonances for isomers A and C are nearly the same as are these resonances for isomers B and D. As given in Table 4, A and C have acac methyl singlets at 2.05 and 2.04 ppm and for B and D these values are 2.24 and 2.27 ppm respectively. Isomers of the same idealized geometry have been shown by Juhala for [Co(NTA)(tfa)] to have very similar anisotropies for protons in the molecule which are far removed from C-O bond anisotropic deshielding effects.[62] In other words the trans-N-C_2 isomers of $[Co(acac)_2(S\text{-ala})]$ would be expected to have similar total magnetic environments as would the cis-N-C_2 isomers, but between the two geometries this environment can be different. Since A and C have similar acac methyl resonances as do isomers B and D, pmr can be used to support the assignment of geometric pairs obtained by visible absorption spectroscopy.

A crystal field model was used to assign geometric structures to the C_2 diastereomeric pairs of $[Co(acac)(S\text{-ala})_2]$. It has been found for the systems, $[Co(ox)(S\text{-ala})_2]^-$,[38] $[Co(ox)(gly)_2]^-$,[68, 86] $[Co(ox)(S\text{-ser})_2]^-$,[43] $[Co(ox)(\quad\text{-ala})_2]^-$,[87] $[Co(ada)_2]^-$[88] and $[Co(mal)(gly)_2]^-$,[68] that the trans-N geometry exhibits a splitting (i.e., a shoulder) of the long wavelength visible absorption band whereas cis-N geometry shows no such splitting. Also the trans-N isomers exhibit a higher energy

(shorter wavelength) absorption maxima than do the cis-N isomers for this absorption band.

No splitting of the long wavelength visible absorption band was observed for any of the C_2 isomers of [Co(acac)(S-ala)$_2$]. Therefore the split band criteria cannot be used to assign the trans-N geometry in this system. However, isomers A and C of [Co(acac)(S-ala)$_2$] exhibit a long wavelength visible absorption maxima at 524 nm or at higher energy than isomers B and D which absorb at 570 nm. Hence by analogy to the above systems the diastereomeric pair A and C is assigned trans-N-C_2 geometry and the B and C pair is assigned cis-N-C_2 geometry. Failure to observe the split band has led other researchers to incorrectly assign the structure of an isomer of [Co(acac)(S-ala)$_2$][65] (probably because they did not isolate all six isomers of the system).

Chiral assignments by PMR for the trans-N-C_2 diastereomers

Isomers A and C of [Co(acac)(S-ala)$_2$] were assigned trans-N-C_2 geometry above and only at this point can the chirality of these diastereomers be predicted on the basis of pmr chemical shift arguments. Values for the chemical shifts of the isomers are given in Table 4.

Isomer C exhibits a methine proton quartet resonance for coordinated S-ala at 3.91 ppm or downfield relative to the corresponding methine resonance of isomer A which is center at 3.77 ppm. Space filling molecular models reveal that Λ -trans-N-C_2-[Co(acac)(S-ala)$_2$] places

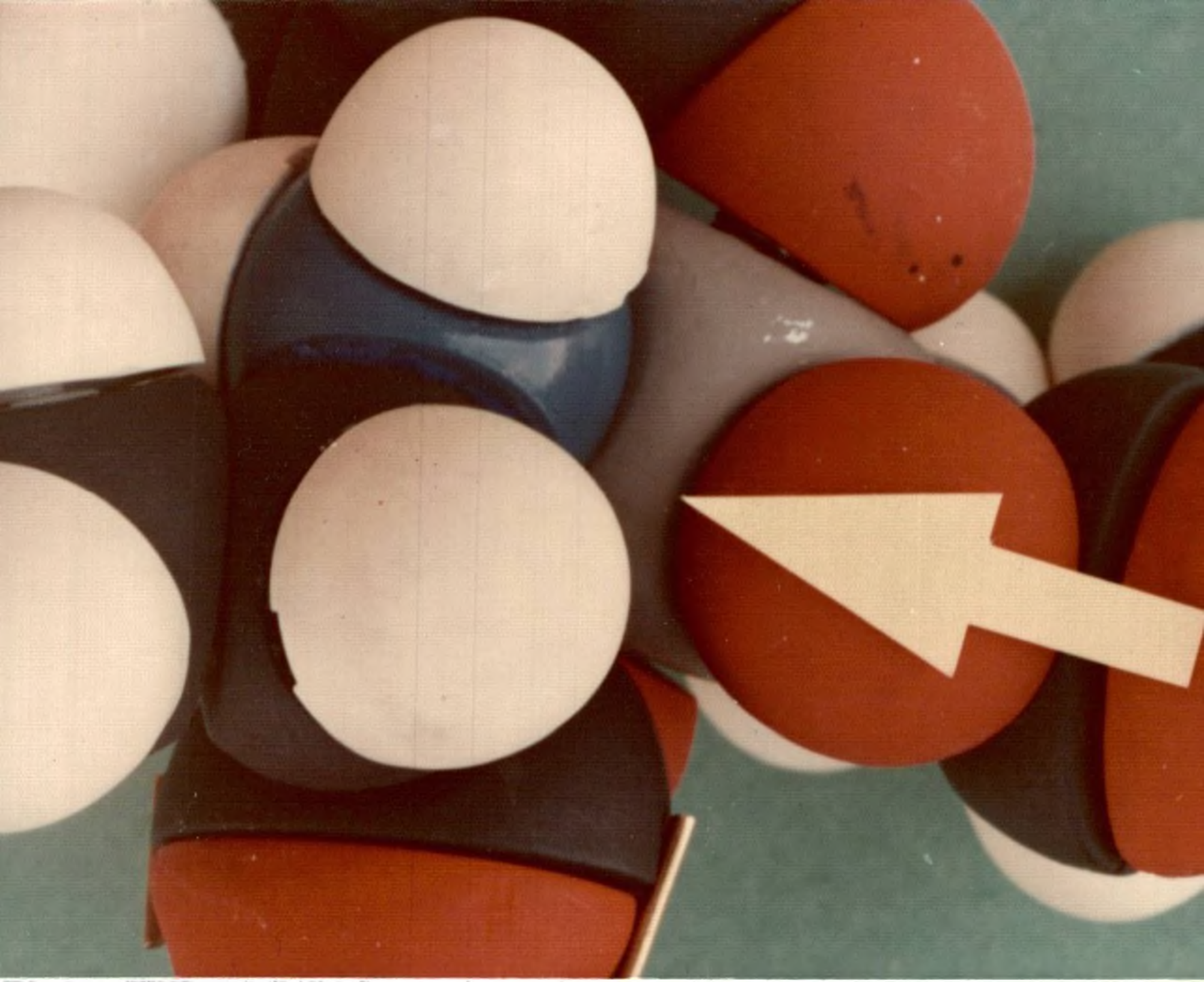
the S-ala methine proton directly in line with the C-O bond of an adjacent acac ligand as shown in Figure 18. Models also show that △ -trans-N-C_2-[Co(acac)(S-ala)$_2$] places the methine proton of S-ala above the C-O bond of a coordinated acac ligand as shown in Figure 19. In both cases only one S-ala methine need be shown because the complexes have C_2 symmetry and thus the S-ala ligands are chemically and magnetically equivalent. Applying bond anisotropic deshielding arguments, a Λ helix for this complex is predicted to exhibit a deshielded S-ala methine proton relative to a △ helix. On this basis, isomer C with the downfield S-ala methine resonance is assigned Λ helix and isomer A is assigned a △ helix.

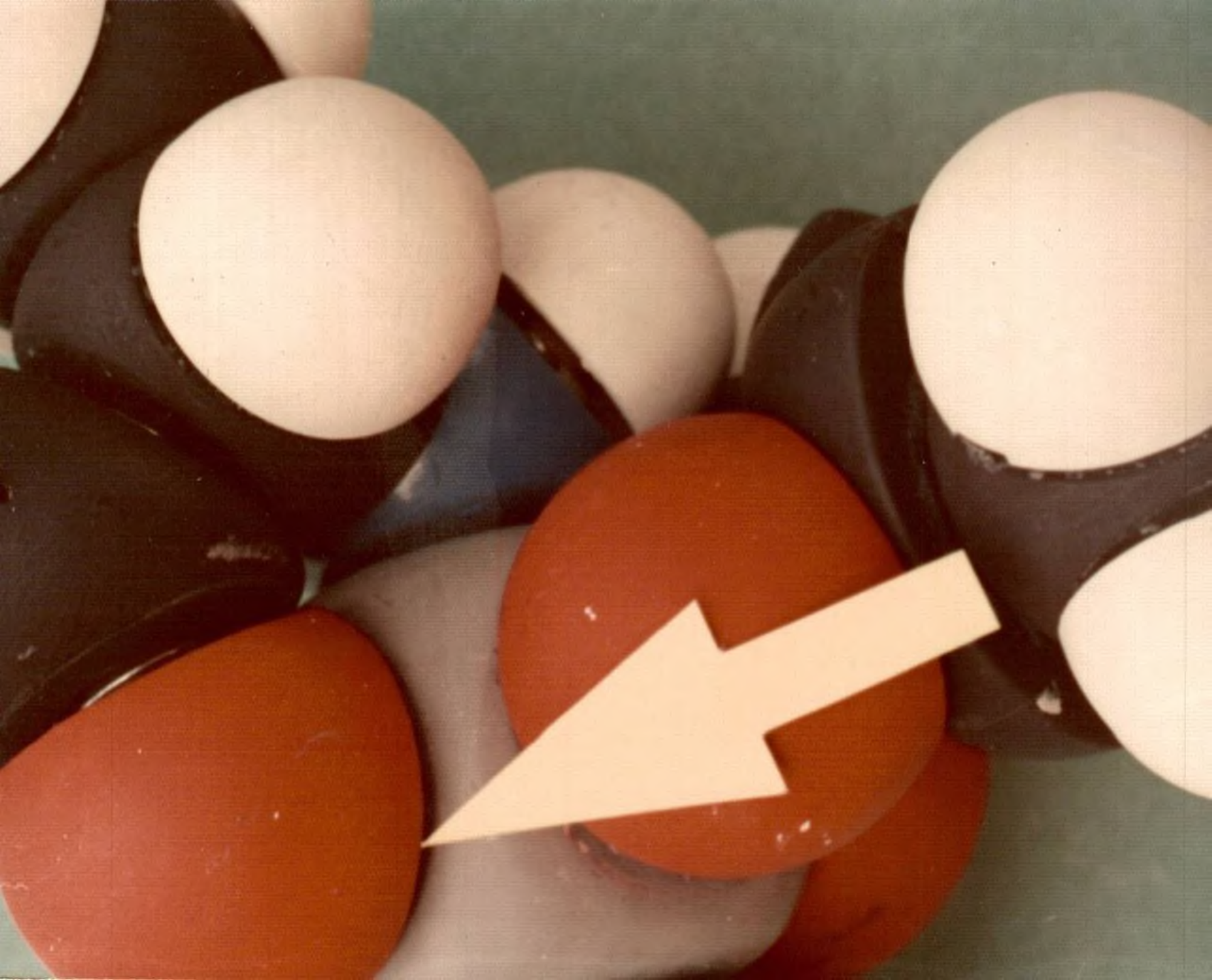
Isomer C exhibits a pmr methyl doublet resonance for the S-ala ligand centered at 1.51 ppm and isomer A exhibits a corresponding doublet resonance centered at 1.57 ppm. Thus in isomer A the methyl group of S-ala is downfield by 0.06 ppm relative to isomer C. Figure 20 shows the methyl group of S-ala in a △ helix of this system is in line with a C-O bond of an adjacent acac ligand. Figure 21 shows the Λ helix for this system places the methyl group of S-ala above the C-O bond of an adjacent acac ligand.

Bond anisotropy predicts a deshielded methyl resonance for S-ala in △ -trans-N-C_2-[Co(acac)(S-ala)$_2$] relative to the Λ isomer. Thus isomer A with the downfield S-ala methyl resonance can be assigned the △ chirality and isomer C is assigned a Λ chirality. This is in

Fig. 18.--Methine proton of S-ala in Λ -trans-N-C_2-[Co(acac)-S-ala)$_2$] in line with a C-O bond of the acac ligand.

Fig. 19.--Methine proton of S-ala in Δ -trans-N-C_2-[Co(acac)-S-ala)$_2$] above a C-O bond of the acac ligand.





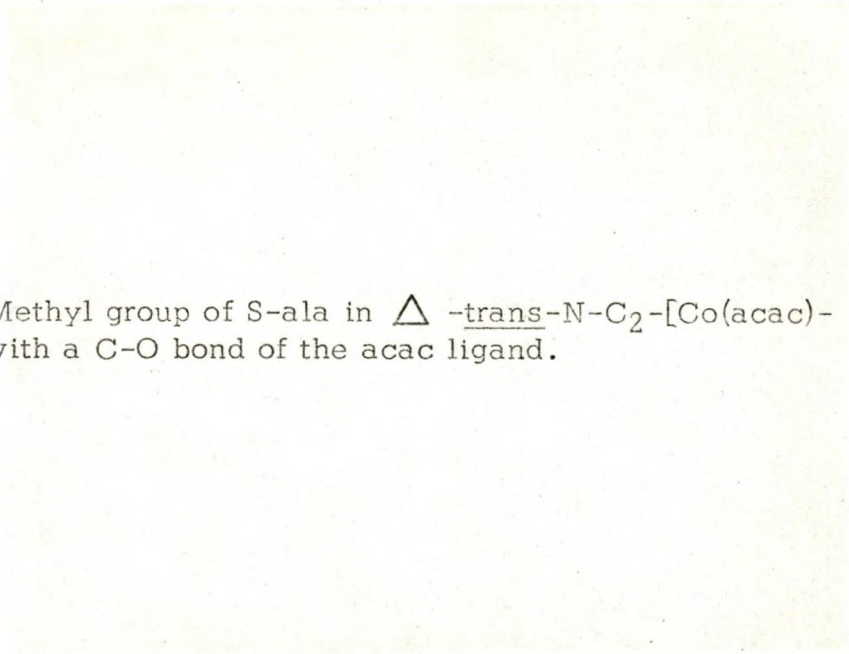


Fig. 20.--Methyl group of S-ala in Δ -trans-N-C_2-[Co(acac)-S-ala)$_2$] in line with a C-O bond of the acac ligand.

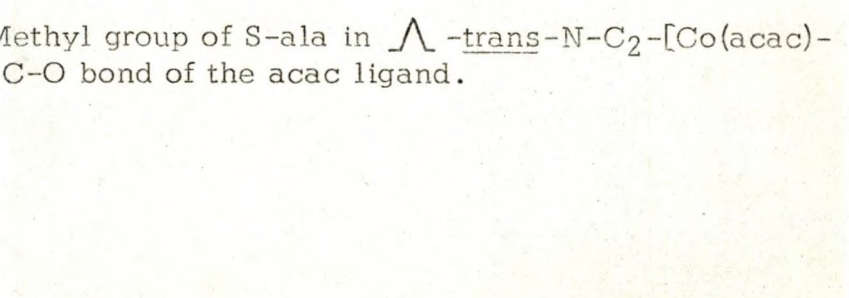
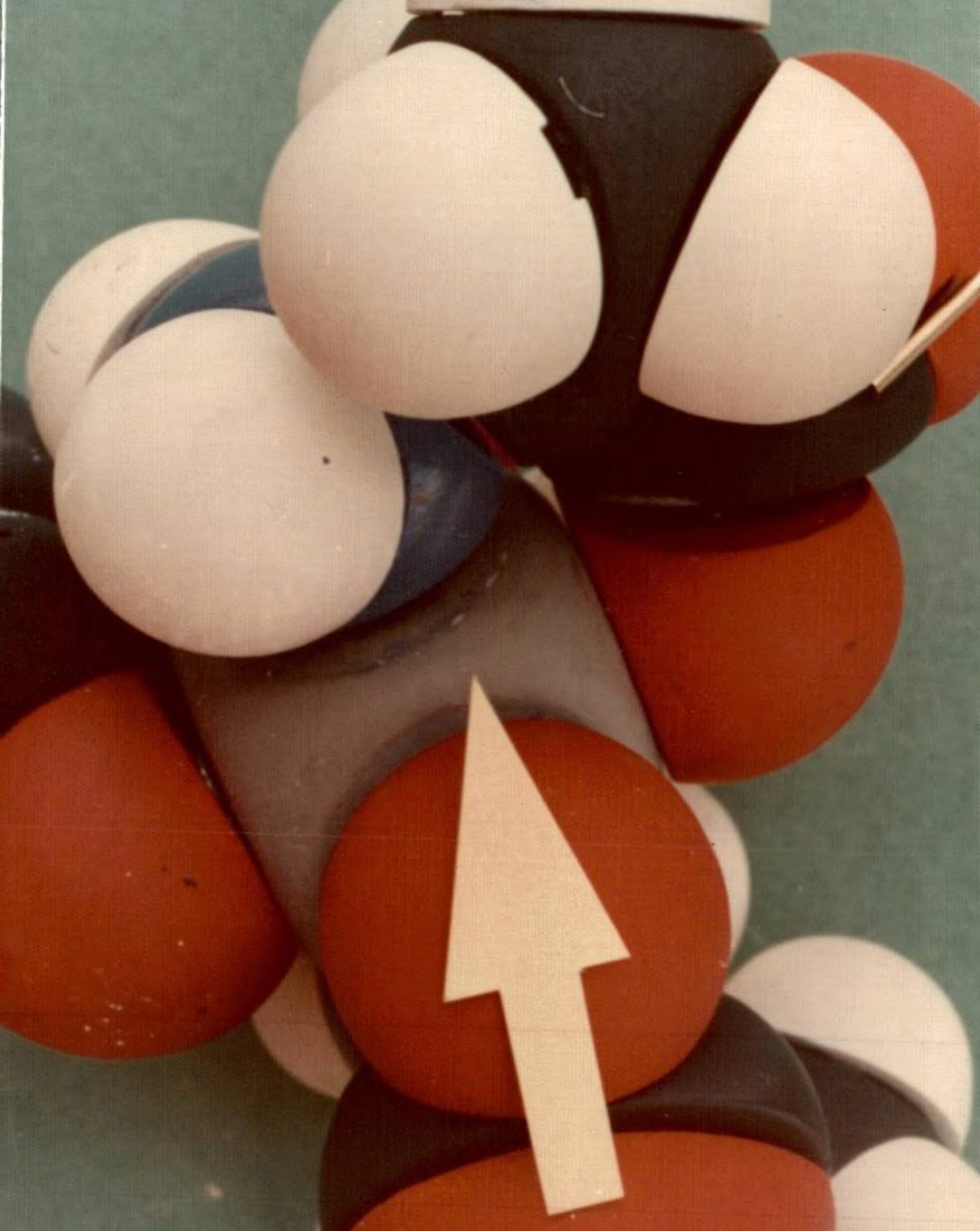


Fig. 21.--Methyl group of S-ala in Λ -trans-N-C_2-[Co(acac)-S-ala)$_2$] above a C-O bond of the acac ligand.



agreement with predictions made above from the relative chemical shifts of the S-ala methine proton.

The chemical shift of the S-ala methyl groups for the diastereomers is smaller (0.06 ppm) than the chemical shift for the methine protons (0.14 ppm). This is to be expected since the methyl groups are in a pseudo equatorial position on the chelate ring and thus farther from the source of the anisotropic deshielding than the pseudo axial methine protons.

Chiral assignments
by the CD method

Visible CD spectra, as illustrated in Appendix II, show a large positive long wavelength absorption band for isomer C indicative of a Λ helix and a large negative absorption band for isomer A indicating a Δ helix (see Table 5).[14] Thus pmr and CD chiral assignments for the diastereomers of trans-N-C_2-[Co(acac)(S-ala)$_2$] are in agreement.

Chiral assignments by PMR for
the cis-N-C_2 diastereomers

For the system [Co(acac)(S-ala)$_2$], isomers B and D were assigned cis-N-C_2 geometry from visible absorption spectroscopy as discussed previously. Since the isomers are diastereomeric, bond anisotropic deshielding arguments and pmr chemical shifts can be used to make chiral assignments.

TABLE 5

CHIRAL ASSIGNMENTS FOR THE ISOMERS OF $[Co(acac)(S\text{-}ala)_2]$

Isomer	Pmr Assignment	Major Sign of CD Band[a]	CD Assignment
A. trans-N-C_2	Δ	(-)	Δ
B. cis-N-C_2	Λ	(+)	Λ
C. trans-N-C_2	Λ	(+)	Λ
D. cis-N-C_2	Δ	(-)	Δ
E. cis-N-C_1	Δ	(-)	Δ
F. cis-N-C_1	Λ	(+)	Λ

[a]Sign indicates the sign of the dominant CD band in the long wavelength region as measured in water.

Chemical shift values are reported for isomers B and D in Table 4. Isomer B exhibits an S-ala methine quartet resonance at 3.87 ppm which is downfield from the corresponding methine resonance of isomer D at 3.76 ppm. The S-ala methyl signal resonates at 1.44 ppm for isomer B and at 1.54 ppm for isomer D. Thus isomer B has a deshielded S-ala methine and a shielded S-ala methyl resonance relative to D.

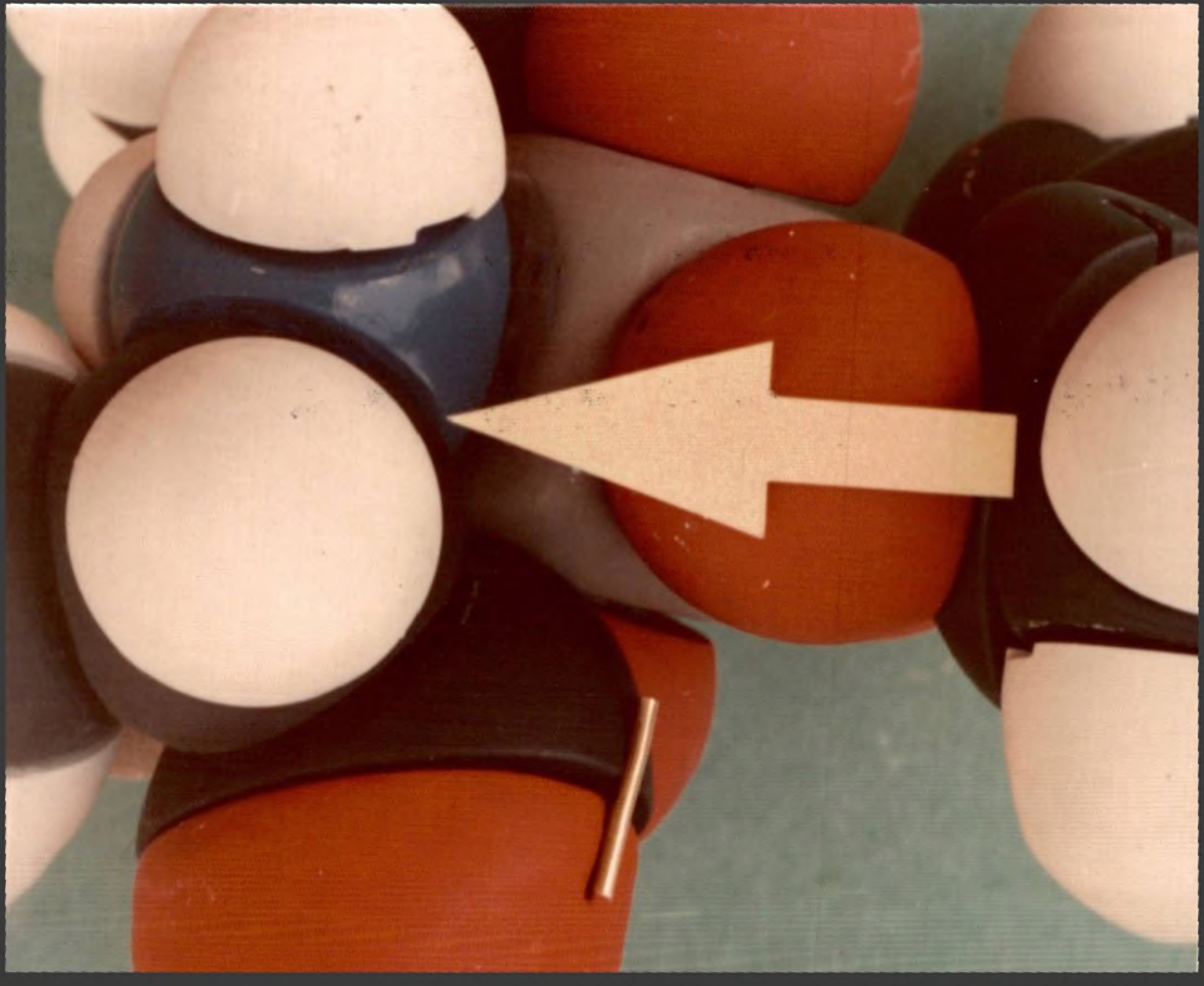
Examination of space filling molecular models reveals that Λ-cis-N-C_2-[Co(acac)(S-ala)$_2$] places the methine proton of S-ala in line with the C-O bond of an adjacent acac ligand as shown in Figure 22. A Δ helix for this system reveals the S-ala methine is in line with an N-D bond of the adjacent amino acid ligand shown in Figure 23. In the Λ helix the S-ala methine is deshielded by a C-O bond, however, in the Δ chirality the methine is also deshielded, in this case by N-D steric compression.[20]

Figure 24 illustrates that a Λ helix for the system places the methyl group of S-ala in line with an N-D bond of the other S-ala ring. This would cause the methyl group to be deshielded by steric compression.[20] In the Δ configuration the S-ala methyl group is in line with a C-O bond of an adjacent acac ligand also in a deshielded position as shown in Figure 25.

Thus the diastereomers of cis-N-C_2-[Co(acac)(S-ala)$_2$] present a situation in which the methine and methyl groups of S-ala are predicted to be deshielded in both chiral forms of the complex. Pmr chemical shifts

Fig. 22.--Methine proton of S-ala in Λ -cis-N-C_2-[Co(acac)-S-ala)$_2$] in line with a C-O bond of the acac ligand.

Fig. 23.--Methine proton of S-ala in Δ -cis-N-C_2-[Co(acac)-S-ala)$_2$] in line with an N-D bond of the adjacent S-ala ligand.



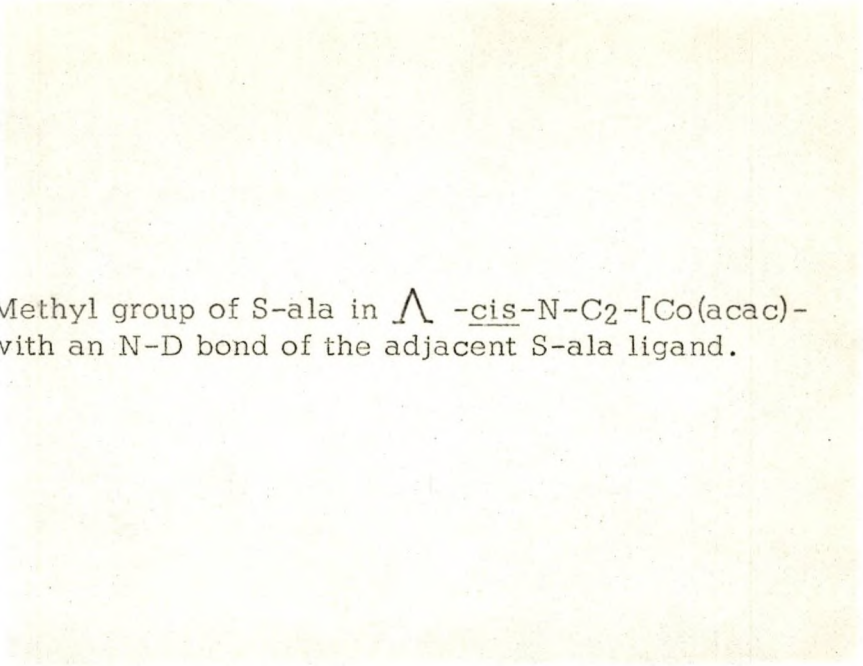


Fig. 24.--Methyl group of S-ala in Λ -cis-N-C_2-[Co(acac)-S-ala)$_2$] in line with an N-D bond of the adjacent S-ala ligand.

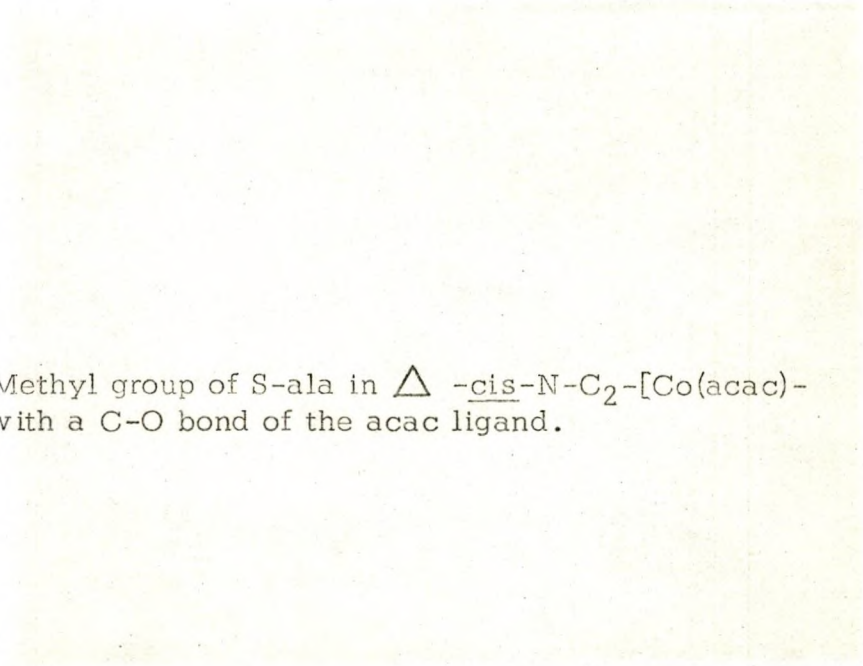


Fig. 25.--Methyl group of S-ala in Δ -cis-N-C_2-[Co(acac)-S-ala)$_2$] in line with a C-O bond of the acac ligand.

for the diastereomers indicate, however, that one of the sources of deshielding must be more effective than the other due to the methine being downfield in isomer B and the methyl group resonating downfield in isomer D.

Berends found that for the Δ and Λ chiral forms of cis-N-C_2-$[Co(ox)(S\text{-ala})_2]^-$, C-O bond anisotropy was more effective than N-D steric compression in deshielding the protons of the S-ala ligand.[42] Berends' conclusion is logical if one considers the character of a C-O bond of coordinated acac. X-ray data shows that the C-O bond length of an acac ligand is approximately 1.26 A for several systems studied.[22] This bond length is similar to the carbonyl bond length in simple aldehydes and ketones.[89] Qualitatively it is presumed that the C-O bond of an acac ligand possesses double bond character and therefore would exhibit a much stronger magnetic anisotropy than an N-D single bond.[90]

From these observations, isomer B of $[Co(acac)(S\text{-ala})_2]$ with the downfield methine resonance for S-ala, is assigned the Λ helix. Isomer D which exhibits a more downfield methyl resonance for S-ala is thus assigned a Δ helix.

Chiral assignments
by the CD method

Isomer B exhibits a positive long wavelength visible CD band indicative of a Λ helix and isomer D exhibits a negative long

wavelength visible CD curve indicative of a Δ helix (see Table 5 and Appendix II).[14] Thus the pmr and CD chiral assignments are in agreement for the isomers of this system.

Chiral assignments by PMR of the cis-N-C_1 diastereomers

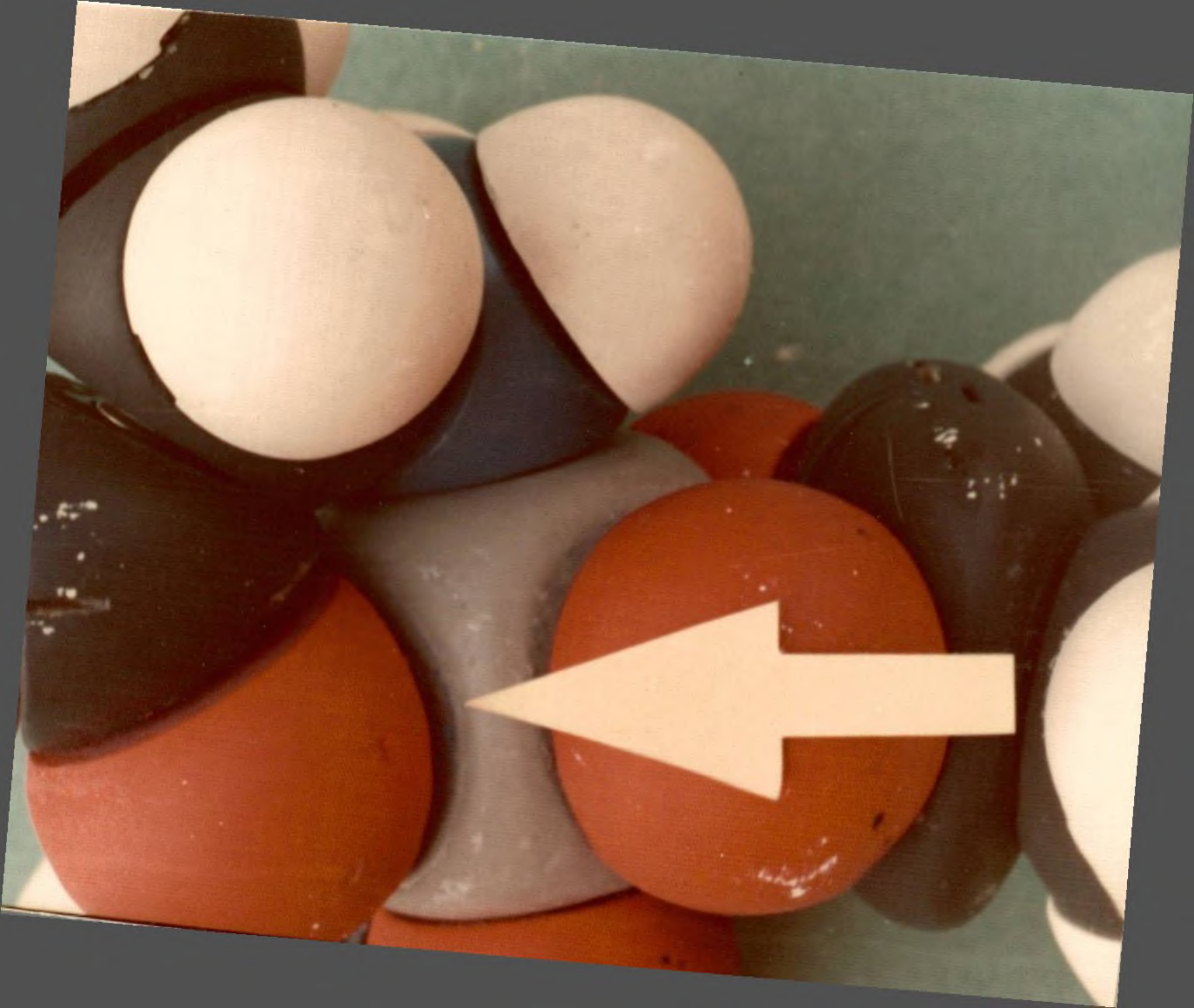
Isomers E and F of the system [Co(acac)(S-ala)$_2$] were shown previously to possess cis-N-C_1 geometry from their pmr spectra. Since the isomers are diastereomers with the same geometry, pmr arguments may be used to make chiral assignments. The pmr chemical shifts for the ligands in isomers E and F are given in Table 4.

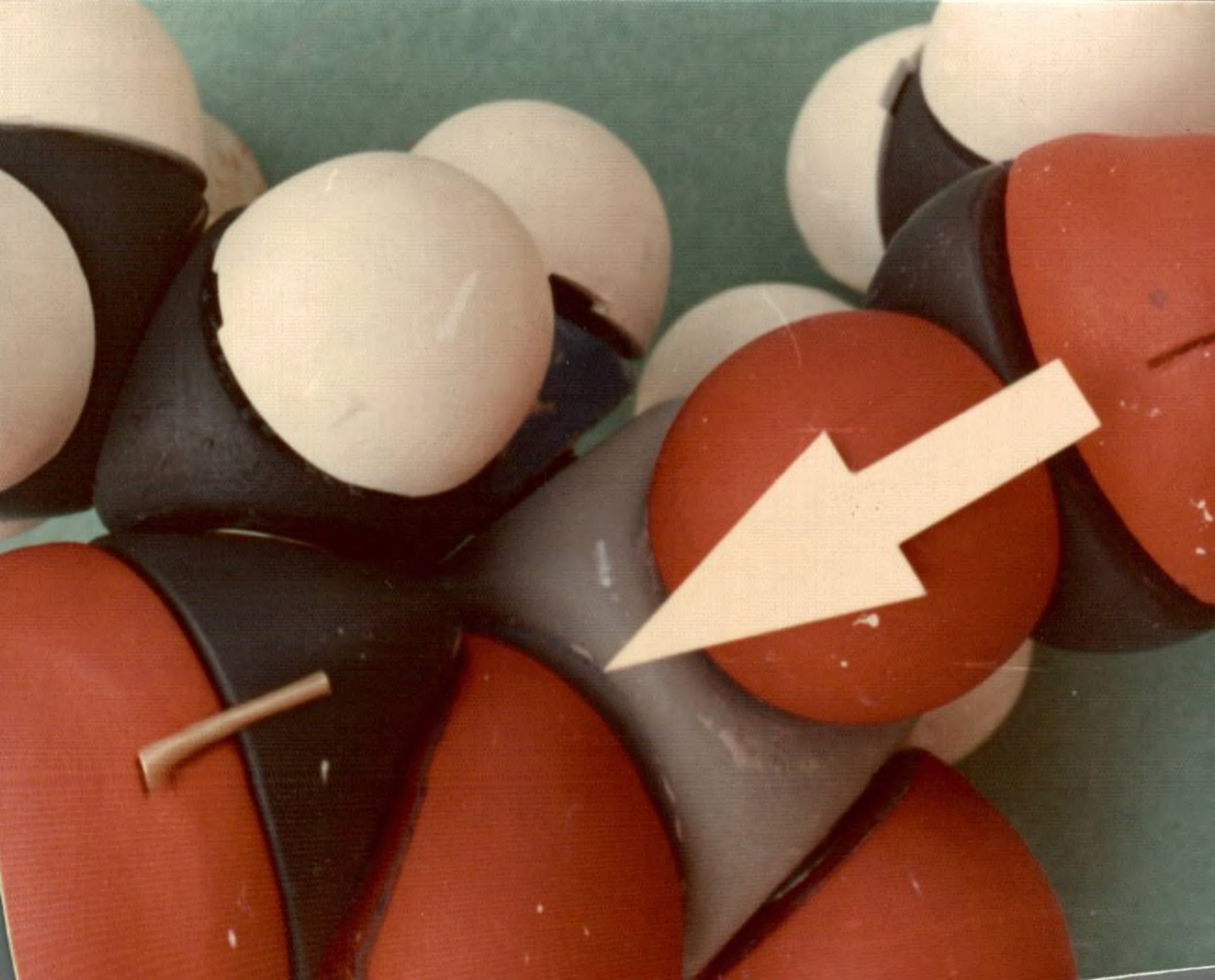
Isomer E exhibits methine resonances for the non-equivalent S-ala ligands at 3.52 and 3.70 ppm. Isomer F exhibits resonances for the corresponding methine protons at 3.66 and 3.81 ppm. Therefore isomer F contains the most downfield methine (3.81 ppm) resonance signal. The non-equivalent methyl groups for the S-ala ligand appear at 1.39 and 1.51 ppm in isomer E and at 1.40 and 1.47 ppm in isomer F. Thus isomer E exhibits the most downfield methyl resonance (1.51 ppm).

Inspection of space filling molecular models reveals that Δ-cis-N-C_1-[Co(acac)(S-ala)$_2$] contains two situations for the non-equivalent methine protons of the S-ala ligands. As shown in Figure 26, one methine is above the C-O bond of an adjacent acac ligand and as shown in Figure 27, the other methine is above the C-O bond of an adjacent S-ala ligand. For Λ-cis-N-C_1-[Co(acac)(S-ala)$_2$] the

Fig. 26.--Methine proton of an S-ala ligand in Δ -cis-N-C_1-Co(acac)$(S\text{-ala})_2$] above a C-O bond of the acac ligand.

Fig. 27.--Methine proton of an S-ala ligand in Δ -cis-N-C_1-Co(acac)$(S\text{-ala})_2$] above the C-O bond of the adjacent S-ala ligand.



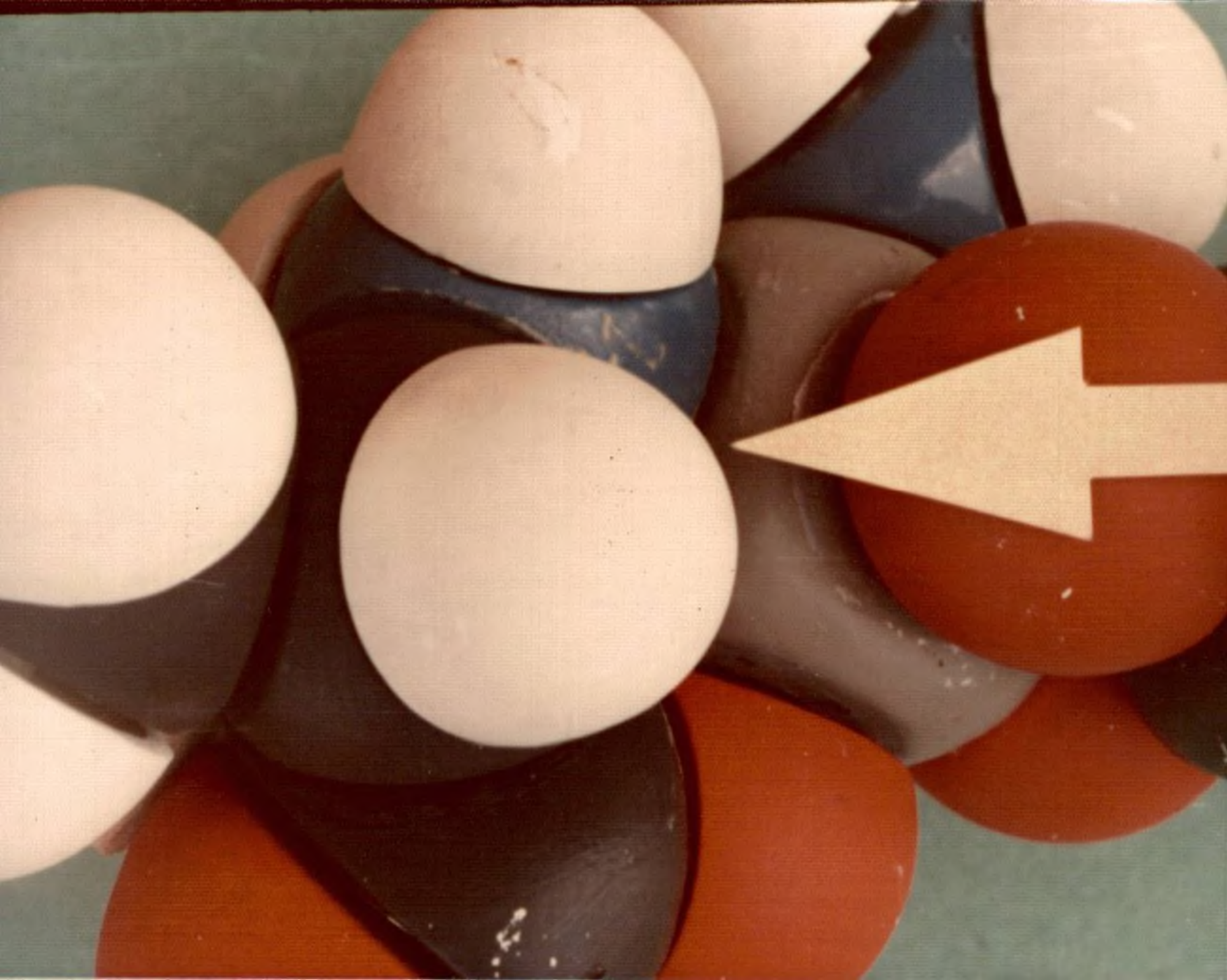


methine protons are shown in Figures 28 and 29. The methine proton in Figure 28 lies between the N-D bonds of the adjacent S-ala ligand, while in Figure 29, the methine is in line with the C-O bond of the adjacent acac ligand. Thus only Λ-cis-N-C_1-[Co(acac)(S-ala)$_2$] contains a methine proton of S-ala that is predicted to be deshielded by C-O bond anisotropy (see Figure 29). This is easily seen since in the Δ helix, the S-ala methine protons, as shown in Figures 26 and 27, are both shielded by C-O bond anisotropy. In Figure 28, one S-ala methine in the Λ helix is not sterically compressed by an N-D bond and is therefore not deshielded,[20] however, the other methine in the Λ isomer is deshielded by C-O bond anisotropy as shown in Figure 29. On this basis isomer F which exhibits the most downfield methine resonance of S-ala is assigned a Λ helix. Isomer E is therefore assigned a Δ helix. Wingert et al.,[21] used a similar argument to assign the diastereomers of cis-N-C_1-[Co(acac)(S-val)$_2$]. Interestingly, the chiral assignments of the cis-N-C_1-[Co(ox)(S-ala)$_2$]$^-$ system studied by Berends are consistent with this reasoning, but the argument presented by Berends would incorrectly assign the chirality of the [Co(acac)(S-ala)$_2$] and [Co(acac)(S-val)$_2$] C_1 diastereomers.[42]

The situations for the non-equivalent methyl groups of the S-ala ligands in Δ-cis-N-C_1-[Co(acac)(S-ala)$_2$] are shown in Figures 30 and 31. In Figure 30 the methyl group lies between two N-D bonds of the adjacent S-ala ligand which is not expected to be a deshielded

Fig. 28.--Methine proton of an S-ala ligand in Λ-cis-N-C_1-[Co(acac)(S-ala)$_2$] between the N-D bonds of the adjacent S-ala ligand.

Fig. 29.--Methine proton of an S-ala ligand in Λ -cis-N-C_1-[Co(acac)(S-ala)$_2$] in line with a C-O bond of the acac ligand.



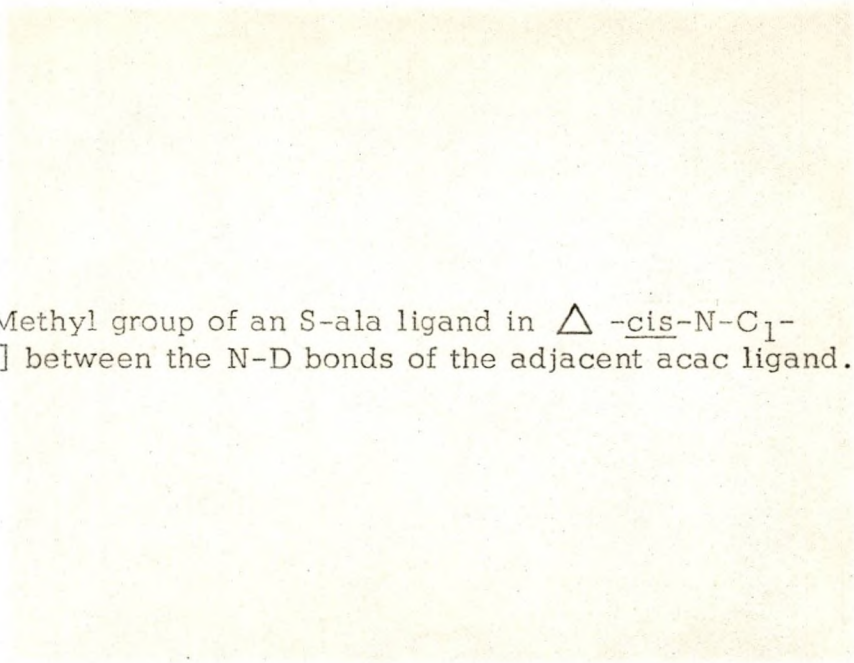
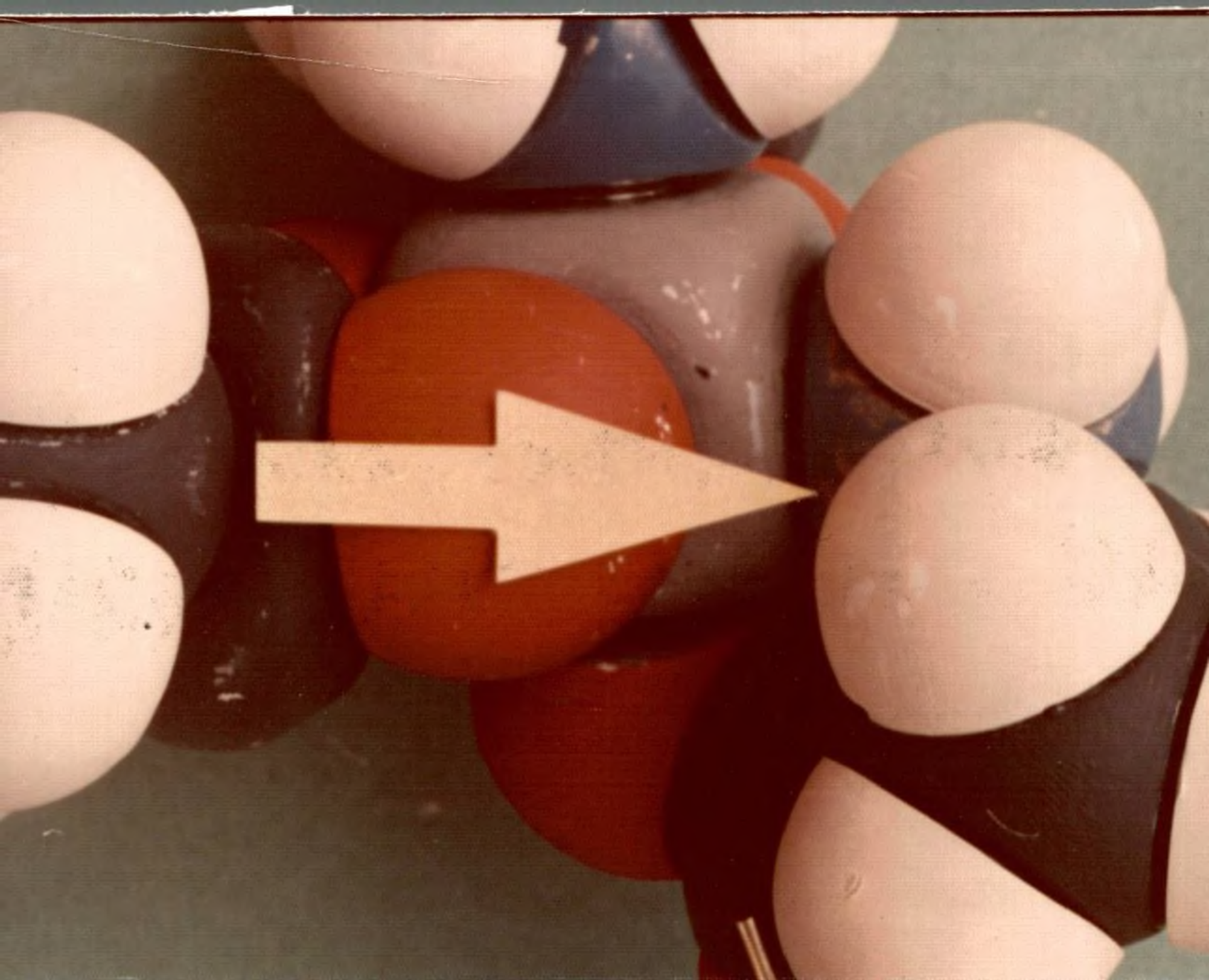


Fig. 30.--Methyl group of an S-ala ligand in △ -cis-N-C_1-[Co(acac)(S-ala)$_2$] between the N-D bonds of the adjacent acac ligand.

Fig. 31.--Methyl group of an S-ala ligand in △ -cis-N-C_1-[Co(acac)(S-ala)$_2$] in line with a C-O bond of the acac ligand.



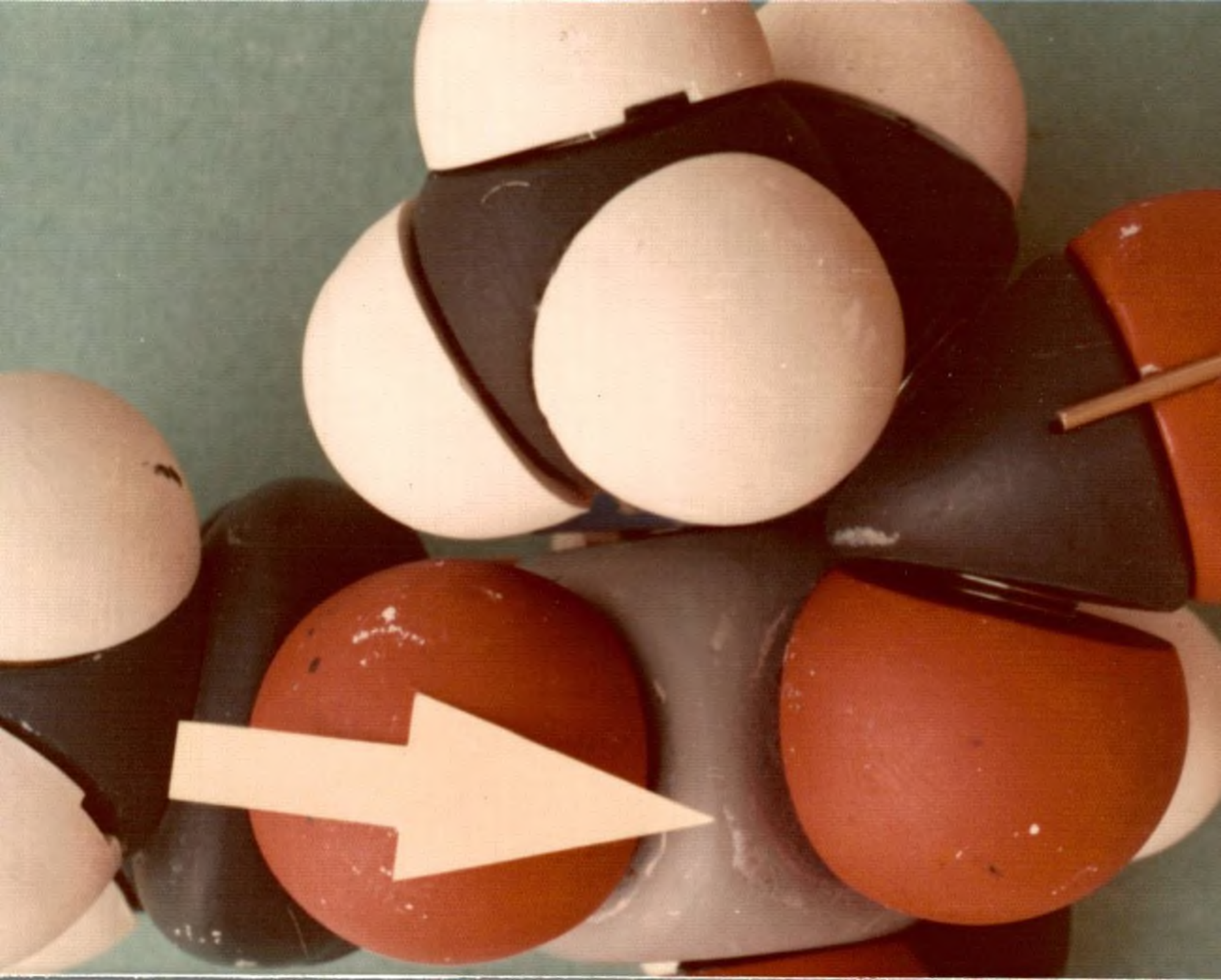
environment. However, the methyl group shown in Figure 31 is in line with the C-O bond of the adjacent acac ligand in a relatively deshielded environment. For the Λ-cis-N-C_1 isomer the methyl groups are shown in Figures 32 and 33. In both cases for a Λ helix the methyl groups are in relatively shielded environments. Therefore Δ-cis-N-C_1-[Co(acac)(S-ala)$_2$] would be expected to exhibit the most deshielded S-ala methyl resonance. From Table 4 it can be seen that isomer E, which was assigned a Δ helix above, exhibits the most downfield S-ala methyl resonance. Thus chiral assignments made from the S-ala methine and methyl group chemical shifts are in agreement.

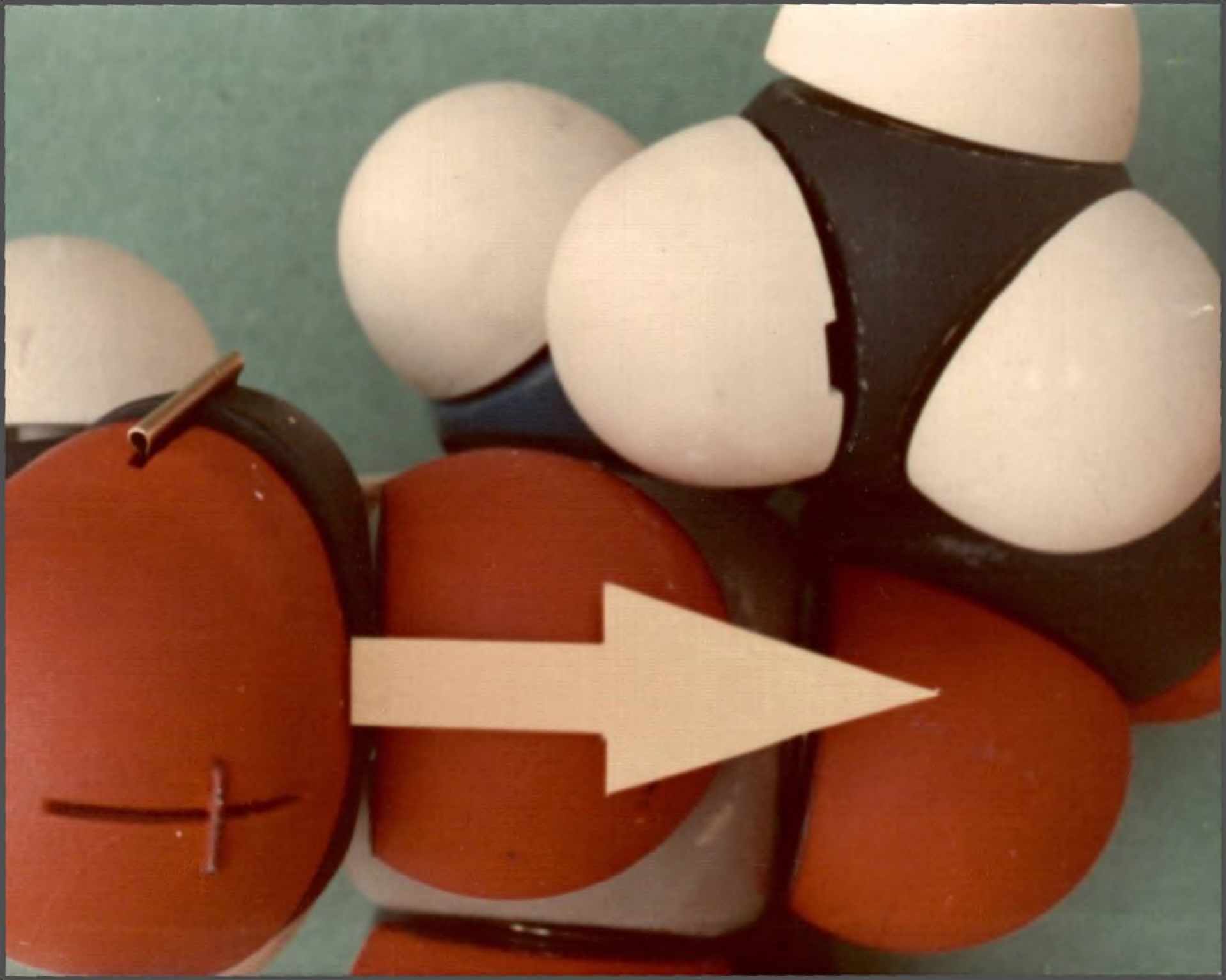
Chiral assignments
by the CD method

Visible CD spectra show a large negative long wavelength CD band for isomer E indicating a Δ helix and for isomer F a large positive CD band indicating a Λ helix (see Table 5 and Appendix II).[14] Again the pmr and CD chiral assignments are in agreement.

Fig. 32.--Methyl group of an S-ala ligand in Λ -cis-N-C_1-[Co(acac)(S-ala)$_2$] above a C-O bond of the acac ligand.

Fig. 33.--Methyl group of an S-ala ligand in Λ -cis-N-C_1-Co(acac)(S-ala)$_2$] above the C-O bond of the adjacent S-ala ligand.





CONCLUSIONS

1. The separation and structural assignments of fourteen previously unknown diastereomers for the system $[Co(acac)_n(S\text{-amac})_{3-n}]$ where n = 1 or 2 are reported. The diastereomers are soluble in chloroform, acetone, ethanol and water.

2. The pmr C-O bond magnetic anisotropic deshielding model is a simple, fast and reliable method for determining the chirality of tris-chelate $Co(NO_5)$ and $Co(N_2O_4)$ diastereomeric complexes. In every case studied the pmr method is in agreement with the optical CD method for making the chiral assignments.

3. The magnetic anisotropy of a C-O bond is more effective than N-D steric compression as a source of proton deshielding in the Δ and Λ-cis-N-C_2-$[Co(acac)(S\text{-ala})_2]$ diastereomers.

4. The argument presented by Berends for assigning chirality to the cis-N-C_1-$[Co(ox)(S\text{-ala})_2]^-$ diastereomers by pmr has been simplified and generalized in order to account for the results obtained for the diastereomers of $[Co(acac)(S\text{-ala})_2]$.

5. Chemical shifts that can be predicted by the C-O bond model are not dependent upon hydrogen bonding solvents or ionic strength of the media surrounding the metal complexes.

6. Helical diastereomeric complexes possess no great differences in their total magnetic environments that are not explainable by bond anisotropies.

7. Complexes of the type $[Co(acac)_2(S\text{-amac})]$ do not exhibit any stereospecificity caused by non-bonded interactions while $[Co(ox)_2(S\text{-amac})]^{2-}$ complexes are quite sensitive to this phenomenon.

8. A previously unknown high yield, one step synthesis for the complex $[Rh(acac)_3]$ from $RhCl_3 \cdot 3H_2O$ has been developed. This procedure has since been used by Everett in the preparation of $[Rh((+)_D\text{-}3\text{-acetylcamphorate})_3]$.[48]

APPENDICES

APPENDIX I

LIST OF ABBREVIATIONS

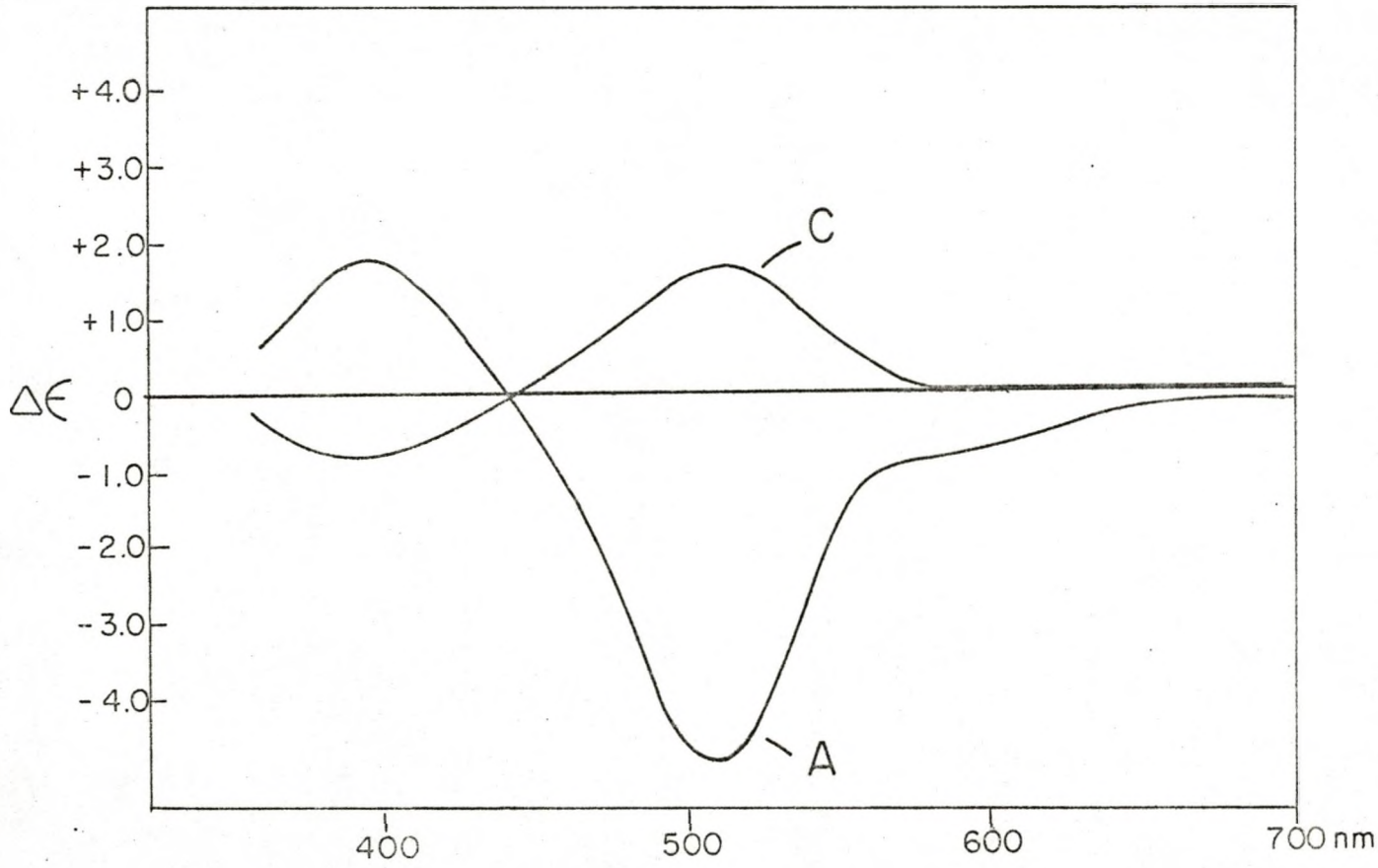
LIST OF ABBREVIATIONS

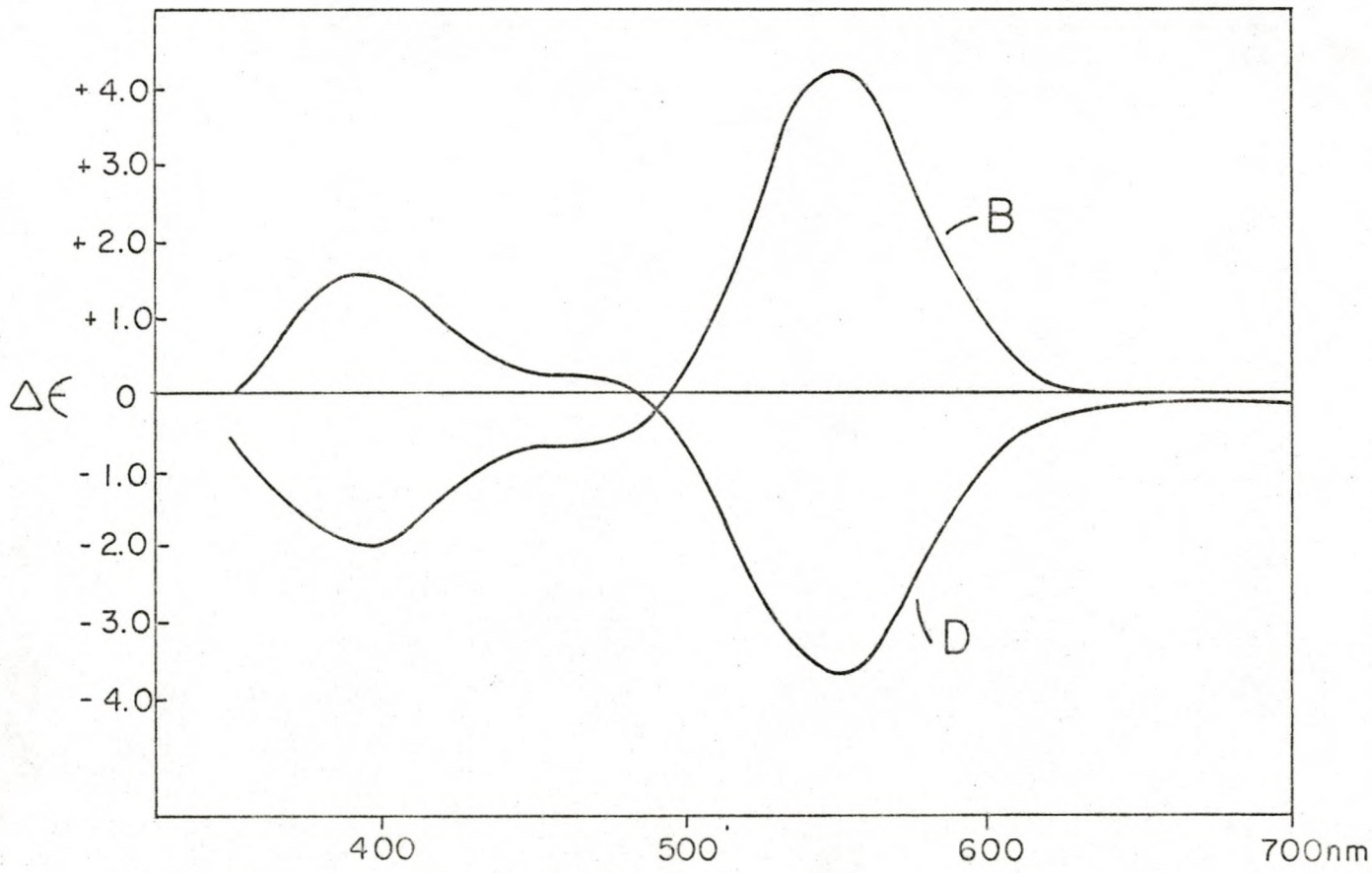
en	ethylenediamine
EDTA	ethylenediaminetetraacetate ion
acac	2,4-pentanedione enolate ion
ox	oxalate ion
hfa	1,1,1,5,5,5-hexafluoro(2,4-pentanedione) enolate ion
dipy	2,2'-bipyridine
o-phen	1,10-phenanthroline
gly	glycine ion
tfa	1,1,1-trifluro(2,4-pentanedione) enolate ion
ibn	2,2-dimethylethylenediamine
pn	2-methylethylenediamine
S-ala	S-alanine ion
S-ser	S-serine ion
S-val	S-valine ion
N-me-S-ala	N-methyl-S-alanine ion
mal	malonate ion
glu	glutamate ion
EDDA	ethylenediaminediacetate ion

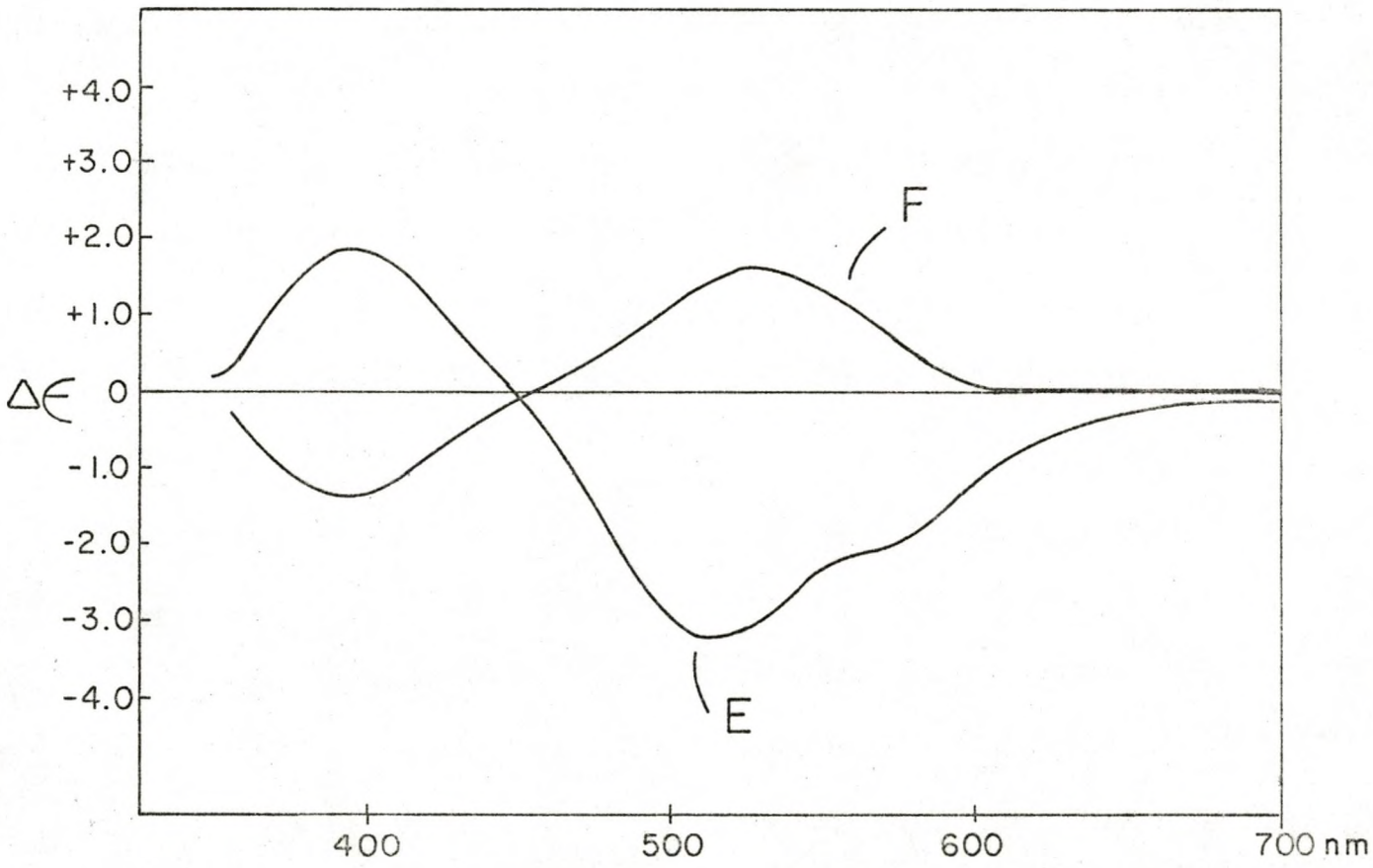
N,N'-dimeen	N,N'-dimethylethylenediamine
NTA	nitrilotriacetate ion
sarc	sarcosine ion
N-me-S-val	N-methyl-S-valine ion
S-pro	S-proline ion
2S,3R-thr	2S,3R,threonine ion
β -ala	β -alanine ion
ada	aminodiacetate ion

APPENDIX II

CD CURVES


+4.0
+3.0
+2.0
+1.0
ΔE 0
-1.0
-2.0
-3.0
-4.0
C
A
400
500
600
700 nm


+ 4.0
+ 3.0
+ 2.0
+ 1.0
Δε 0
- 1.0
- 2.0
- 3.0
- 4.0
B
D
400
500
600
700nm


+4.0
+3.0
+2.0
+1.0
Δε 0
-1.0
-2.0
-3.0
-4.0
F
E
400
500
600
700 nm

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